ABSTRACTS OF WORLD MEDICINE

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Pathology

EXPERIMENTAL AND CHEMICAL PATHOLOGY

1. The Effect of Experimental Cerebral Infarction on Transaminase Activity in Serum, Cerebrospinal Fluid and Infarcted Tissue

K. G. WAKIM and G. A. FLEISHER. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **31**, 391–399, June 27, 1956. 2 figs., 13 refs.

In studies carried out at the Mayo Clinic it was shown that the production of experimental cerebral infarction in dogs by the aseptic injection of 0·2 ml. of vinyl acetate into the internal carotid artery led to an increase in glutamic oxalacetic transaminase activity in the cerebrospinal fluid, the mean value rising from 0·66 μM. per hour per ml. of fluid to 5·5 μM. after infarction; the transaminase activity was greatest about 100 hours after infarction and remained above pre-infarction level for 15 days. The increase in enzymatic activity (which averaged 733%) was proportional to the severity and extent of the cerebral infarction.

Transaminase activity in the serum increased from a mean of 1·05 to 2·2 μM. per hour per ml. (average increase 110%); besides being less than that for cerebrospinal fluid, the rise was not proportional to the extent and severity of infarction, and did not begin so soon after it. The transaminase activity in infarcted cerebral tissue was considerably less than that in normal brain (0·94 μM. compared with 3·21 μM. per hour per mg. of tissue), indicating that the release of transaminase from infarcted cerebral tissues was responsible for the enhanced enzymatic activity of the cerebrospinal fluid and serum. The authors suggest that determination of the transaminase activity of the cerebrospinal fluid might be of value in the diagnosis of damage to cerebral tissue. *J. E. Page*

2. Variation of Plasma Electrolyte and Total Protein Levels in the Individual

J. K. FAWCETT and V. WYNN. *British Medical Journal* [*Brit. med. J.*] **2**, 582–585, Sept. 8, 1956. 3 figs., 9 refs.

The authors have investigated, at St. Mary's Hospital, London, the diurnal and temporal variations in the plasma concentrations of sodium, potassium, chloride, total carbon dioxide, and total protein in healthy young persons of both sexes. Comparison of the results in 25 men with those in 25 women (mean values and standard deviations are given in tabular form) showed that there was no sex difference in regard to potassium or total protein, but in women the sodium level was lower, the chloride level higher, and the total carbon dioxide concentration lower than in men. In a long-term study samples of blood were taken on 10 occasions over 2 to 6 months from 4 healthy men and 4 healthy women. Subsequent determinations showed that the variation in electrolyte values in one individual at different times was less than that between different individuals in the case of potassium, chloride, total carbon dioxide, and total protein, but not in respect of sodium. The variation in the plasma electrolyte levels during the day were also studied in 5 young men, but no definite pattern of change emerged. A study carried out during the menstrual cycle in 3 young women showed that menstruation had an influence on the plasma electrolyte levels, but had no effect on the plasma protein concentration.

It is pointed out that the plasma levels of potassium, chloride, CO_2, and total protein tend to be characteristic of the individual, and therefore values generally regarded as " normal " may be outside the normal range of some individuals. *C. L. Cope*

3. Urine and Serum Mucoproteins in Cancer and Other Diseases

E. LOCKEY, A. J. ANDERSON, and N. F. MACLAGAN. *British Journal of Cancer* [*Brit. J. Cancer*] **10**, 209–221, March, 1956 [received July, 1956]. 8 figs., 22 refs.

In patients suffering from cancer the serum concentration of mucoprotein is above normal, but this increase is not specific for malignant diseases. In this paper from the Westminster Hospital, London, a study is reported of the serum and urinary concentrations of mucoproteins in 63 healthy subjects, 114 patients with cancer, and 215 patients with other diseases. There was a close correlation between the mucoprotein levels in the urine and serum, suggesting that the urinary mucoproteins originate in part in the blood. Both urinary and serum levels were frequently above normal in cancer, but similar elevations were also seen in inflammatory and the collagen diseases. Very high values were observed mainly in cases of cancer, the highest being recorded in patients with disseminated disease, whether primary or secondary. The levels were markedly raised in cases of lymphoma, but in malignant disease mainly confined to bone very little increase was noted. In other neoplastic diseases the levels were intermediate.

After surgical treatment there was generally a marked rise in the mucoprotein levels. The effect of radio-

therapy, however, was inconstant, but there was some indication that a fall in the serum concentration of mucoprotein was related to a favourable clinical response.

L. A. Elson

4. Cholesterol in Serum and Lipoprotein Fractions: Its Measurement and Stability

J. T. ANDERSON and A. KEYS. *Clinical Chemistry* [*Clin. Chem.*] **2**, 145–159, June, 1956. 10 refs.

In view of the potential importance of β-lipoprotein cholesterol in the pathogenesis of atherosclerosis, the determination of its concentration in the serum, as well as that of total cholesterol, seems desirable in the study of this problem. In this paper from the University of Minnesota, Minneapolis, methods are described for the estimation of total cholesterol in 0·1-ml. samples of serum and its fractionation into α- and β-lipoprotein cholesterol.

The serum is hydrolysed with 2% potassium hydroxide solution in ethanol for not less than 90 minutes at 37° C., the cholesterol extracted three times with petroleum ether and water, and a drop of 25% acetic acid in petroleum ether added to the combined extracts, which are then evaporated to dryness in a colorimeter tube by directing a stream of warm air into the tube, Liebermann–Burchard reagent is then added to the dry residue and, after 20 minutes, readings are taken in a photo-electric absorptiometer with a 620-mμ filter at 5-minute intervals until a maximum is reached. Standard and blank samples are put through the same process. This method, which is an adaptation of the method of Abell *et al.*, gives reproducible results which are slightly higher than those given by digitonin methods, but about 20% lower than the values given by the Bloor extraction method, in which the total cholesterol is measured without preliminary hydrolysis. However, by this last method the ester cholesterol is measured together with the free cholesterol, so that the value given for free cholesterol content is erroneously high.

The amounts of cholesterol associated with the α and β lipoproteins of the serum are determined after separation of the protein fractions by paper electrophoresis in veronal buffer at *p*H 8·6. Two strips are used for each sample, one being stained with Sudan Black B to indicate the position of the lipoprotein fractions, and the corresponding areas of the other being cut out and their cholesterol content determined separately by the method described above. In normal subjects replicates gave good agreement and the results compared well with those obtained directly by cold ethanol precipitation. Agreement was not so good when serum from patients with abnormal cholesterol metabolism was used. It is pointed out that serum cholesterol determinations are unreliable if carried out on serum which has been stored at room or refrigerator temperature. It was shown, however, that serum which has been air-dried on filter paper yields reliable results even after many months.

The fasting serum cholesterol level was determined by this method in 22 healthy, and 13 obese but otherwise healthy, young men taking a constant diet, and the estimation repeated after one week. The mean values from all estimations in the two groups were 209·5 and 214·3 mg. per 100 ml. respectively, there being considerable variation between the individual values obtained on the two occasions. In a group of 24 ambulant middle-aged men with coronary heart disease two readings at an interval of 3 months gave a mean total cholesterol level of 273·4 mg. per 100 ml., and again there was much individual variation between the two readings.

M. Lubran

5. Serum Iron Determination

G. R. KINGSLEY and G. GETCHELL. *Clinical Chemistry* [*Clin. Chem.*] **2**, 175–183, June, 1956. 5 figs., 8 refs.

An improved method of serum iron determination is described in this paper from the University of California and the Veterans Administration Center, Los Angeles, based on the fact that 4:7-diphenyl-1:10-phenanthroline forms a highly coloured complex with ferrous iron which is soluble in *iso*-amyl alcohol. The reagent is used as a 0·0025-M solution in *iso*-amyl alcohol. A 1-ml. sample of serum is mixed with 3 ml. of water and 2 ml. of N hydrochloric acid and heated for 30 minutes in a boiling water-bath. After cooling, 2 ml. of saturated sodium acetate solution, 6 ml. of the colour reagent, and 0·5 ml. of saturated hydrazine sulphate solution are added and the mixture shaken vigorously for 2 minutes by hand and centrifuged. A 5-ml. sample of the *iso*-amyl alcohol layer is then clarified with 0·5 ml. of ethanol and a reading taken in a photo-electric absorptiometer at 540 mμ. A reagent blank and standards are treated simultaneously.

The serum iron concentration (in μg. per 100 ml.) as determined by this method in healthy subjects 20 to 60 years old were: for females (12 subjects) 120 to 200 (mean 182); for males (13 subjects) 125 to 238 (mean 160).

M. Lubran

6. Recent Clinical Experience with Serum Aminopherase (Transaminase) Determinations

J. M. MERRILL, J. LEMLEY-STONE, J. T. GRACE, and G. R. MENEELY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1454–1456, April 28, 1956. 4 figs., 2 refs.

The serum transaminase (glutamic oxalacetic aminopherase) level was estimated in patients with various diseases at the Veterans Administration Hospital (Vanderbilt University School of Medicine), Nashville, Tennessee. The serum level of the enzyme in healthy control subjects [number unstated] ranged from 10 to 45 units per ml. of serum.

In all cases of acute myocardial infarction the level was increased to 3 to 12 times the normal, falling to normal values in 2 to 4 days. In one patient with acute rheumatic pericarditis, however, there was only a slight temporary elevation, the level falling to normal after administration of cortisone, and normal values were invariably found in other types of heart disease, including angina of effort, calcific aortic stenosis, chronic rheumatic valvulitis, acute pulmonary oedema with hypertensive cardiovascular disease, auricular flutter of 48 hours' duration, left bundle-branch block, old healed

cardiac infarction, arteriosclerotic heart disease, and idiopathic benign pericarditis.

Raised serum enzyme levels were found in 2 patients with muscle necrosis resulting from ischaemia due to arterial disease. The level was also found to be increased during exploratory thoracotomy [in an unstated number of patients] and remained so for periods of 2 days to 2 weeks afterwards; this again may have been owing to muscle injury. High serum levels (56 to 1,900 units per ml.) were found in 20 patients with jaundice due to cirrhosis, carcinoma of the pancreas, acute and chronic hepatitis, and infarction of the liver or other abdominal viscera. The serum enzyme levels in liver disease could be correlated with the serum protein levels, the amount of cephalin flocculation and thymol turbidity, the prothrombin time, the serum cholesterol, alkaline-phosphatase, and bilirubin levels, and with the degree of cellular necrosis demonstrated by liver biopsy. Transaminase was found in the bile in concentrations of 25 to 60 units per ml., and the serum levels remained fairly constant in cases of extrahepatic obstruction with a progressive rise in the serum bilirubin level, suggesting that regurgitation of bile was not a major source of the high serum enzyme levels found in liver disease.

Robert de Mowbray

7. **Griess' Nitrite Test in Diagnosis of Urinary Infection**

R. SCHAUS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 528–529, June 9, 1956. 11 refs.

In the nitrite test, first proposed by the German chemist Griess in 1879 for testing the purity of water supplies (and since considerably modified) a red colour due to the presence of nitrite develops on the addition of an acidic sulphanilic-acid-α-naphthylamine reagent to contaminated water, certain bacteria breaking down nitrate to nitrite. The test has been used clinically in the past in the diagnosis of urinary infection and the present author, writing from Washington University School of Medicine, St. Louis, hopes to revive interest in it.

After giving some details of the preparation of the reagent and commenting on its instability he describes the method. This consists in adding to a few ml. of fresh urine one-quarter of its volume of reagent; if nitrite is present a red colour develops almost instantaneously, and is not affected by excess of protein or phosphates. False positive results are said to occur only if the urine has been exposed to bacterial contamination after voiding, and a positive result may be obtained in cases of bacteriuria alone, without pyuria. Unfortunately not all bacteria are capable of reducing nitrate, but of those which do *Escherichia coli* is the most notable; staphylococci and *Proteus vulgaris* do so to a lesser extent, while the *Salmonella* group of organisms are inconstant in action. False negative results are therefore very likely, even in the presence of nitrate-reducing organisms, and may be due to various causes, such as deterioration of the reagent, the absence of nitrate in the urine, marked polyuria, or retention of urine (in which case the nitrite already produced may have been further decomposed, particularly in the presence of *E. coli*).

[Although the author is of the opinion that this simple test is of value in routine urine analysis, it appears to the abstracter to confer no advantages, since direct examination and culture of the urine are still necessary whether the test result is negative or positive.] *P. I. Reed*

HAEMATOLOGY

8. **Electron Microscopy of Thin Sections of Reticulocytes.** [In English]

A. BRUNNER, A. VALLEJO-FREIRE, and P. SOUZA SANTOS. *Experientia* [*Experientia (Basel)*] **12**, 255–257, July 15, 1956. 5 figs., 12 refs.

Thin sections of blood cells from guinea-pigs in which reticulocytosis had been induced by bleeding 3 days previously were examined by electron microscopy at the Butantan Institute, São Paulo, Brazil. The reticulocytes were readily distinguished from mature erythrocytes and were shown to contain lamellated filaments with a limiting membrane. This structure, which is characteristic of mitochondria, and the fact that the filaments were stained by mitochondrial stains indicate, in the authors' opinion, that the reticular formation is of mitochondrial origin. They found that the appearance of these bodies was influenced by changes in the concentration of salts in the fixation medium, presumably owing to osmotic effects.

Marjorie Le Vay

9. **Biological Interaction between Lymphocytes and Other Cells**

J. G. HUMBLE, W. H. W. JAYNE, and R. J. V. PULVERTAFT. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 283–294, July, 1956. 15 figs., 11 refs.

At Westminster Medical School, London, the authors have applied the techniques of serum-agar culture and phase-contrast time-lapse cinemicrography to a study of approximately 300 specimens of human bone marrow, of a similar number of human lymph nodes, of numerous samples of pleural and ascitic fluid, and many specimens of primary and secondary malignant tumours; in addition, murine bone marrow, malignant tissue, and exudates were similarly studied. The methods and materials are described.

Lymphocytes were seen to wander at random until they came into touch with a malignant cell or a megakaryocyte, when they began to move round the cell, adhere to it, or penetrate it. Occasionally one or several lymphocytes penetrated a cell and appeared to remain alive and to move within it. The lymphocytes did not appear, however, to be attracted to malignant cells as polymorphonuclear granulocytes are to bacteria. Another peculiar phenomenon which was often observed was the passage of a lymphocyte across the narrow cytoplasmic bridge of a cell in the late stage of mitosis —an appearance which the authors liken to the cutting of the umbilical cord.

The name suggested for these phenomena is the Greek compound word emperipolesis—"inside round-about

wandering". No other type of cell was found to have these properties. It is suggested that lymphocytes further the growth and division of cells, regardless of their nature, and that in malignant disease this mechanism acts to the disadvantage of the host. *T. B. Begg*

10. **Phospholipids from Brain Tissue as Accelerators and Inhibitors of Blood Coagulation**
P. BARKHAN, M. J. NEWLANDS, and F. WILD. *Lancet* [*Lancet*] **2**, 234, Aug. 4, 1956. 11 refs.

In view of the current interest in the problem of the relation of lipids to atherosclerosis and blood coagulation the authors present, from the University of Cambridge, this preliminary communication on the chemical fractionation of human brain tissue and the effects of various fractions on the thromboplastin generation test, the antithromboplastin test, and the accelerated clotting time of blood, using Russell's viper venom. They found that of the two fractions showing greatest activity, one probably consisting chiefly of phosphatidyl serine was an inhibitor of coagulation, and the other, probably mainly phosphatidyl ethanolamine, was an accelerator of coagulation. *A. Brown*

11. **Food Lipids and Blood Coagulation**
N. F. MACLAGAN and J. D. BILLIMORIA. *Lancet* [*Lancet*] **2**, 235–236, Aug. 4, 1956. 9 refs.

In the study of the relationship between dietary fats and blood coagulation here reported from Westminster Hospital Medical School, London, the minimum amount of each of a number of common fatty foods required to produce maximum shortening of the accelerated clotting time of the blood (using "stypven") when added to 0·2 ml. of normal plasma was defined as one "clotting unit". Strongly positive results were confined almost solely to milk products, and ranged from 5,000 clotting units per 100 g. for butter to less than 100 units per 100 g. for various brands of margarine and for lard. The active principle was found in the lower turbid aqueous layer of the centrifuged melted fats. These results seem to suggest that the effect on coagulation is not related only to the induced plasma turbidity due to chylomicra, but also to the activity of a closely related group of phospholipids present mainly in milk products. *A. Brown*

12. **The Assay of Antihaemophilic Globulin (AHG) in Plasma**
W. R. PITNEY. *British Journal of Haematology* [*Brit. J. Haemat.*] **2**, 250–264, July, 1956. 8 figs., 23 refs.

This report from the Postgraduate Medical School of London describes a new method of assaying antihaemophilic globulin (AHG) in normal subjects and in haemophiliacs which is based on a modification of the thromboplastin generation test. The method differs from that of Biggs *et al.* (*Brit. J. Haemat.*, 1955, **1**, 20; *Abstracts of World Medicine*, 1955, **18**, 92) principally in its use of fresh human plasma as the normal standard (instead of freeze-dried ox-plasma concentrate) and of aluminium-hydroxide-treated plasma from a severe case of haemophilia as the source of Factor V (instead of a freeze-dried fraction of normal plasma). It is thought that these modifications will bring the test within the scope of smaller laboratories engaged in routine work.

The assay of AHG allows the diagnosis of haemophilia to be established in mild cases of the disease in which the clotting time is normal and even thromboplastin generation is normal, or only slightly abnormal. Of 36 cases of haemophilia investigated, the AHG concentration was less than 1% in 21 cases and did not exceed 25% in the other 15, whereas in 30 normal subjects the value ranged from 50 to 220%. Investigation of the rate of loss of AHG activity in citrated normal plasma stored at 4° C. showed that about half this activity was lost in 24 hours and that thereafter the rate of loss followed an exponential pattern.

[This test seems suitable for adoption on a fairly wide scale. The original paper should be consulted by all those interested in the technical details.] *T. B. Begg*

MORBID ANATOMY AND CYTOLOGY

13. **Pulmonary Changes in Leukaemic Patients after Modern Methods of Treatment.** (Изменения в легких при лейкозах, подвергавшихся современным методам лечения)
A. D. SOBOLEVA. *Архив Патологии* [*Arkh. Patol.*] **18**, 54–56, No. 1, 1956. 5 refs.

The lungs of patients dying of leukaemia after treatment with urethane, *x* rays, or "embikhin" show a total absence of the usual leukaemic leucostasis and lymphatic involvement. Destructive changes are present, as a rule, in the walls of blood vessels, and these are often thrombosed. This is associated with pulmonary infarction, exudation of plasma, and massive haemolysis (after "embikhin" treatment). Amorphous protein material and so-called "amyloid" bodies are seen lying free in the alveoli. *L. Crome*

14. **Pathogenesis of Endocardial Fibro-elastosis**
W. J. S. STILL and E. H. BOULT. *Lancet* [*Lancet*] **2**, 117–118, July 21, 1956. 6 figs., 11 refs.

The aetiology and pathology of congenital endocardial fibro-elastosis remain obscure. At the Royal Victoria Infirmary, Newcastle upon Tyne, heart tissue from 6 uncomplicated cases in infants aged 6 to 9 months was examined under the electron microscope. It was found that the surface layers of the endocardium were composed almost entirely of fibres morphologically resembling fibrin. The authors state that ordinary histological examination does not reveal evidence of this deposition of fibrin, and that there may be two reasons for this: (1) the fibrin may have been deposited in utero, as suggested by the condition in premature stillborn infants; or (2) the fibrin may be deposited in very thin fibres and immediately incorporated in the endocardium, thus becoming no longer recognizable as fibrin. It is not implied that the incorporation of fibrin accounts for the whole process of endocardial thickening, but it is certainly an important factor in congenital endocardial fibro-elastosis. *A. W. H. Foxell*

15. **Chronic Generalized Myocardial Ischaemia with Advanced Coronary Artery Disease**

W. F. M. FULTON. *British Heart Journal* [*Brit. Heart J.*] **18**, 341–354, July, 1956. 8 figs., 15 refs.

Hearts from 26 cases of advanced coronary arterial disease were studied at the Royal Infirmary, Edinburgh, a special technique being used which included injection of the coronary tree with a bismuth–gelatin preparation, followed by stereoscopic radiography of the intact heart and of the partially dissected heart. In the 4 cases described in detail the patients were over 65 years of age at death, and each had had a history of 10 years or more of unremitting angina; in none of the 4 cases was there any clinical or electrocardiographic evidence of myocardial infarction before the terminal illness. Patches of necrosis and fibrosis scattered evenly throughout the deeper layers of the left ventricular wall were found in each case, but there was no evidence of occlusion of any major coronary vessel at any time. In all 4 cases narrowing of the coronary ostia was observed and radiographs revealed a dense network of vessels throughout the left ventricular muscle. There was free anastomosis between branches of this network, which was supplied by both the right and left coronary arteries. In spite of the florid vascular pattern, all the patients suffered from myocardial ischaemia, which in the course of years had presumably led to the development of new arterial channels, evenly distributing such limited coronary flow as was available. *J. A. Cosh*

16. **Veno-occlusive Disease of the Liver. Essential Pathology**

G. BRAS and K. R. HILL. *Lancet* [*Lancet*] **2**, 161–163, July 28, 1956. 6 figs., 18 refs.

The term veno-occlusive disease of the liver is now proposed for the hepatic condition previously described under the names serous hepatosis and collagenosis. In this paper from University College of the West Indies, Jamaica, the pathology of the condition is discussed on the basis of liver biopsy studies and the findings at necropsy on 23 infants and children.

The disease usually occurs in young children and is characterized by stunted growth, ascites, and hepatomegaly. Acute, subacute, and chronic stages are described. In the acute stage there is blockage of the small- and, to a lesser extent, medium-sized hepatic veins by swelling of the intimal tissues, this at first consisting mainly of oedema, but later becoming organized. There is massive centrilobular congestion, and the macroscopic appearances at this stage are those of a " nutmeg liver ". It would appear that the centrilobular cells perish purely as a result of the congestion. The acute stage is associated with ascites and may subside, leaving only a trace of thickening of the walls of some of the hepatic veins. The subacute stage is characterized by the development of centrilobular fibrosis and a diminished hepatic venous lumen. In the chronic stage there is cirrhosis, which is indistinguishable clinically from any other type of cirrhosis.

The authors state that the resemblance of the hepatic lesions to those seen in cattle poisoned by senecio is striking. The aetiology of veno-occlusive disease is, however, uncertain, and although poisoning by " bush tea ", which is widely consumed for its alleged medicinal value, is the most likely aetiological factor, malnutrition may also play a part. *W. H. Horner Andrews*

17. **Reversible Glomerular Lesions in Toxaemia of Pregnancy**

V. E. POLLACK, C. L. PIRANI, R. M. KARK, R. C. MUEHRCKE, V. C. FREDA, and J. B. NETTLES. *Lancet* [*Lancet*] **2**, 59–62, July 14, 1956. 5 figs., 8 refs.

The renal lesions in 10 patients with toxaemia of pregnancy were studied in tissue specimens obtained by percutaneous needle biopsy. In 9 of the 10 cases biopsy was performed in the last trimester and again after confinement.

Three different types of lesion were observed and are described in this paper: (1) swelling of the glomerular tufts, which, in the authors' view, was probably associated with pre-eclampsia; (2) swelling of the glomerular tufts and thickening of the basement membrane; and (3) predominant vascular sclerosis. Thickening of the basement membrane with vascular changes was considered to be the " pathological counterpart " of essential hypertension with nephrosclerosis. In some cases all three lesions were present and the swelling disappeared post partum, these being cases either of severe eclampsia with permanent vascular damage or of essential hypertension with superimposed pre-eclampsia. *J. B. Wilson*

18. **Nuclear Size and Nuclear: Cytoplasmic Ratio in the Delineation of Atypical Hyperplasia of the Uterine Cervix**

A. G. FORAKER and J. W. REAGAN. *Cancer* [*Cancer (Philad.)*] **9**, 470–479, May–June, 1956. 3 figs., 20 refs.

Nuclear size and nuclear: cytoplasmic ratio in atypical hyperplasia and intraepithelial carcinoma of the uterine cervix have been subjected to measurement and comparison. Nuclear measurements on normal and abnormal epithelium from 20 cases each of intraepithelial carcinoma, atypical hyperplasia, and squamous metaplasia were prepared. The results showed: 1. Little difference in nuclear measurement properties of normal epithelium from all three types of cases. 2. Similar mean nuclear size in all epithelial layers, and similar nuclear: cytoplasmic ratio in the basal layers of intraepithelial carcinoma and atypical hyperplasia. 3. Progressively higher nuclear : cytoplasmic ratio in the middle layer of epithelium in metaplasia, atypical hyperplasia, and intraepithelial carcinoma. 4. Evidence of more cell maturation through the layers of atypical hyperplasia than in those of intraepithelial carcinoma.

With respect to the sum of these nuclear measurement properties, atypical hyperplasia occupied an intermediate position between metaplasia and intraepithelial carcinoma. This intermediate position corresponds to the relationship of the general microscopic pattern of these three entities, as well as to their apparent biological significance in the production of invasive squamous carcinoma of the uterine cervix.—[Authors' summary.]

Microbiology and Parasitology

19. **Prevention of Acute Respiratory Illness in Recruits by Adenovirus (RI–APC–ARD) Vaccine**
M. R. HILLEMAN, R. A. STALLONES, R. L. GAULD, M. S. WARFIELD, and S. A. ANDERSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **92**, 377–383, June, 1956. 1 fig., 18 refs.

Acute respiratory illness caused by the adenovirus (R.I., A.P.C., A.R.D.) family constitutes a major medical problem in recruit training camps of the U.S. Armed Forces. According to the present authors as many as 90% of hospital admissions for respiratory disease during winter months and up to 60% of those during the whole year have been attributed to these viruses. A vaccine was therefore prepared at the Walter Reed Army Institute of Research, Washington, D.C., from tissue cultures of two strains of virus originally isolated from throat washings, and a single dose injected intramuscularly into 311 recruits, 313 others receiving a formol–saline solution for control purposes. During the subsequent observation period of 8 weeks 10·3% of the vaccinated and 28·4% of the control subjects were admitted to hospital with respiratory illness, but when cases occurring during the first week after vaccination were excluded the figures were 4·8% and 23·8% respectively. The number of admissions in each group during the prevaccination period and the first week after vaccination was essentially the same in both groups, whereas from the 2nd to the 4th weeks the number of cases in the control group was 11 times greater than that in the vaccinated group. *Franz Heimann*

20. **Immunogenicity, in Children, of Ultraviolet-treated Poliomyelitis Vaccine**
A. M. WOLF, H. J. SHAUGHNESSY, R. E. CHURCH, A. MILZER, M. JANOTA, F. OPPENHEIMER, R. A. MORRISSEY, H. NAFTULIN, J. W. CHAPMAN, and S. O. LEVINSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 775–781, June 30, 1956. 9 refs.

The authors report the results of the immunization of young children with vaccines prepared from poliomyelitis virus by exposure to ultraviolet radiation. Altogether, about 3,000 children have received vaccine of this type, but the present report is concerned with only a portion of this total, the remainder being still under observation. The vaccines were prepared from several strains of poliomyelitis virus propagated in monkey kidney tissue-cultures and exposed to ultraviolet radiation in thin, flowing films. After rigorous safety tests had ensured that they were free of active virus, different batches of vaccine were injected in three 1- or 2-ml. doses at various intervals into children living in Morgan County, Illinois, where little poliomyelitis had been reported during the last decade so that most of the children had no naturally acquired antibodies in their blood.

The first batch of vaccine was 12 months old when used, and few of the children who received it produced detectable antibodies after the primary inoculation; however, when a booster dose of another batch was given 5 months later antibody levels resulted which were as high as those obtained in other children by primary inoculation with 2-ml. doses of this second batch. Subsequent batches were all shown to be capable of producing satisfactory levels of neutralizing antibodies to all three types of poliomyelitis virus, and in many of the children the antibody level was well maintained for at least a year. A booster dose effectively stimulated a rise in the antibody titre when this had fallen to a low level, but when the level was already high no further rise was observed. Except for one case in which there was a rise of temperature for 24 hours, no reactions have been observed amongst 330 children and there has been no evidence of Rh sensitization of Rh-negative children. Potency tests of the vaccines in monkeys or mice indicated that some were of low antigenicity, but even so they were capable of producing good antibody levels in " immunologically inexperienced " children. *A. Ackroyd*

21. **Comparative Electron-microscopical Studies of the Morphology of *Treponema pallidum, Treponema pertenue*, and Reiter's Spirochaete.** (Vergleichende elektronenmikroskopische Untersuchungen zur Morphologie von Treponema pallidum, Treponema pertenue und Reiterspirochäten)
E. MÖLBERT. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **142**, 510–515, 1956. 9 figs., 6 refs.

Electron-microscopical studies of *Treponema pallidum* by various workers have consistently shown the presence of a narrow band of fibrils running the length of the organism and probably responsible for its motility. The present author, writing from the University of Würzburg, asserts that in pathogenic strains of *T. pallidum* (Nichols and Truffi) and in *T. pertenue* this band, which is about 700 Å wide, constantly contains 6 fibrils, whereas in Reiter's spirochaete there may be between 5 and 12, though 6 is usual. The fibrils show transverse striations similar in appearance to those of collagen fibres.

He has also studied the mechanism of multiplication, which was the same in all the above strains. The point at which fission is to occur is indicated by the formation of a granule of denser material, wider than the body of the organism and traversed by the fibrillar band. This granule then becomes constricted and divides transversely, about half going to each daughter treponeme, in which it appears after division as a terminal granule which later disappears. Dividing forms are most numerous in 7-day-old cultures or in rabbit chancres from the 7th to 10th days, but may still be found after 21 days. Multiplication by spore production does not appear to occur. *M. Lubran*

Pharmacology

22. **Central Effects of Antitussive Drugs on Cough and Respiration**
N. K. CHAKRAVARTY, A. MATALLANA, R. JENSEN, and H. L. BORISON. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **117**, 127–135, June, 1956. 7 figs., 12 refs.

At the University of Utah College of Medicine, Salt Lake City, the authors have investigated the mode of action of the following antitussive drugs: thiopentone sodium, codeine phosphate, dextromethorphan hydrobromide (" romilar "), bis-(1-[carbo-β-dimethylaminoethoxy]-1-phenyl*cyclo*pentane)-ethane disulphone (" toryn "), and sodium 2:6-di-terbutylnaphthalene sulphonate (" becantex "). These were given intravenously to decerebrate or pentobarbitonized cats and their effect on cough, sustained inspiration, and pulmonary ventilation observed, cough and sustained inspiratory responses being elicited by electrical stimulation of the dorsolateral and ventro-medial portions respectively of the medulla oblongata.

All the drugs effectively suppressed cough, but each influenced differently the three aspects of respiration studied. From the selective effects observed the authors discuss the possible neuro-physical mechanisms operating in cough and put forward a hypothesis for antitussive action, as follows. " (1) The cough response represents an activation of a supraregulatory system influencing the basic mechanism concerned in respiratory rhythmicity. (2) Centrally-acting antitussive drugs selectively depress this superimposed activity, leaving the underlying substrate of rhythmic respiration intact." *I. M. Rollo*

23. **Control of Chronic Pain by DL-alpha-Acetylmethadol**
N. A. DAVID, H. J. SEMLER, and P. R. BURGNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 599–603, June 16, 1956. 9 refs.

In the clinical trial here reported from the University of Oregon, Portland, the value of racemic alpha-acetylmethadol hydrochloride (6-di-methylamino-4:4-diphenyl-3-heptanylacetate hydrochloride) for the control of chronic pain was assessed in 76 patients, of whom 49 had cancer, 16 had postoperative or other transient pain, and 11 were suffering from chronic pain due to causes other than cancer; ambulant and bedridden patients were included in the trial. In 13 cases the drug was given by subcutaneous injection and in 63 by mouth only; there was no appreciable difference in the degree or duration of analgesia as between the two methods of administration. The dosage ranged from 5 mg. twice daily to 10 mg. five times a day, depending on the individual patient's requirements; in 2 cases doses of 15 mg. were given terminally. Tolerance and addiction were slow to develop, as shown by the fact that the same dosage could be continued for long periods. Previously administered narcotics (morphine or pethidine) were stopped, or given in reduced dosage, and no withdrawal symptoms resulted.

There was appreciable relief of pain in 20 to 30 minutes after the subcutaneous injection of acetylmethadol and in 40 minutes or less after oral administration, the analgesia lasting 4 or 5 hours. Of the 26 patients who were given the drug for short periods only (2 to 10 days) 21 obtained relief of pain which was as good as or better than that obtained with other narcotics. Of the 50 patients who were treated for longer periods (up to 13 months) 37 experienced excellent or satisfactory relief, 12 required supplementary analgesics, and in only one were the results considered poor. Untoward effects were minimal with small doses. Nausea and vomiting occurred fairly frequently, but it was often difficult to determine the cause, since many of the patients had cancer of the gastro-intestinal tract or metastases in the brain. Moderately severe constipation or even faecal impaction occurred in 10 of the 31 patients receiving more than 30 mg. of acetylmethadol per day, particularly those who were bedridden. Dosage in excess of 20 mg. per day tended to lead to early cumulative effects, manifested by slight depression or the ability to miss doses of the drug, while 6 patients complained of transient dizziness and 13 felt " dopey " or lethargic, particularly if the dose exceeded that required to relieve the pain.

Hypnotics were still required even if 40 or 50 mg. of acetylmethadol was being given per day. Chlorpromazine was found to be a more satisfactory anti-emetic than the antihistaminics, but it did not produce definite potentiation of acetylmethadol. It is concluded that acetylmethadol is a safe and satisfactory analgesic for the control of chronic pain. *T. B. Begg*

24. **Effects of Reserpine on Gastric Secretion**
J. WOLF and M. E. ROSSMAN. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **25**, 430–438, May, 1956. 6 figs., 6 refs.

In investigations carried out at the Veterans Administration Hospital, Bronx, New York, on five groups of patients [the size and composition of which are largely unspecified, but which included 14 patients with known peptic ulcer and others with known gastric hypersecretion] reserpine in a dose of 1·25 mg. given intravenously was shown to be a potent stimulant of gastric acid secretion, its activity being of the same order as that of histamine. Oral administration of 2·5 mg. caused a smaller response. Reserpine-stimulated secretion was not influenced by antihistaminics and anticholinergic drugs. Although the repeated administration of small doses by mouth did not produce a rise in acid secretion, the authors recommend that patients receiving large doses of reserpine over long periods should also be given antacids.

[Insufficient data are provided for the validity of the authors' conclusions to be judged.] *R. Schneider*

Chemotherapy

25. **A Study of the Sensitizing Potential of Novobiocin**
H. WELCH, C. N. LEWIS, L. E. PUTNAM, and W. A. RANDALL. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **3**, 27–32, June, 1956. 1 fig., 11 refs.

Novobiocin has been reported as causing a skin rash in 31 (8·9%) of 348 patients treated by 10 different groups of workers. In this paper from the U.S. Department of Health, Washington, D.C., the authors analyse these reports and find that a rash is likely to occur only when the antibiotic is given in a dosage of 2 g. per day for 6 days or more. In order to confirm this conclusion experimentally 208 adult male volunteer subjects were given 10 g. of novobiocin by mouth over a 12-day period. Only one man developed a drug rash, while in 3 others yellow discoloration of the sclerae was seen which faded slowly after the drug was stopped.

It appears that skin rashes due to novobiocin are the result of too high a dosage for too long a period. In view of the known activity of novobiocin against sensitive organisms and the readiness with which high blood levels can be obtained, the authors suggest that 0·5 g. of the antibiotic twice daily should be an adequate dosage; with such a dosage skin rashes are likely to be limited to less than 1% of patients treated. *I. A. B. Cathie*

26. **Penicillin by Mouth. Laboratory Studies of Absorption of Penicillin V**
M. G. RINSLER and A. C. CUNLIFFE. *Lancet* [*Lancet*] **2**, 328–330, Aug. 18, 1956. 2 figs., 20 refs.

Phenoxymethylpenicillin (" penicillin V ") has been shown to be relatively stable in an acid milieu. In this paper from King's College Hospital and Medical School, London, the authors report the results of laboratory studies of absorption of this antibiotic after oral administration in various doses, and compare the serum penicillin levels with those obtained after oral administration of similar doses of benzylpenicillin. It was assumed that 1 mg. of phenoxymethylpenicillin had an activity approximately equivalent to that of 1,700 units of benzylpenicillin.

The blood penicillin levels after administration of 200,000 units of phenoxymethylpenicillin were in general equal to those attained after twice this dose of benzylpenicillin. The highest level of the latter was usually reached within an hour, but phenoxymethylpenicillin was absorbed more slowly, the peak concentration being reached only after 1 to 2 hours. A detectable amount was maintained in the blood for 4 to 6 hours. One hour after ingestion of 200,000 units of phenoxymethylpenicillin the mean serum penicillin level in 29 healthy volunteers was 1·28 unit per ml., while after a similar dose of benzylpenicillin it was only 0·28 unit per ml., and after 400,000 units it was 0·49 unit per ml. When the serum penicillin levels were plotted against the dose per unit body weight there was a more pronounced rise in the level with an increase in dose of phenoxymethylpenicillin than with benzylpenicillin, but even on a dose/weight basis the range of blood penicillin levels for a given amount of phenoxymethylpenicillin was still very considerable. The total daily dose by mouth of phenoxymethylpenicillin should be at least twice the dose of crystalline penicillin given parenterally.

A. Ackroyd

27. **The Epidemiology of an Erythromycin Resistant Staphylococcus**
A. F. MACCABE and J. C. GOULD. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 223–226, July, 1956. 14 refs.

Since erythromycin has been used with great care and discrimination in Edinburgh hospitals, the emergence of *Staphylococcus aureus* resistant to this antibiotic is considered worthy of report.

A boy aged 9 was admitted to hospital with a 3rd degree burn of the buttock. After excision and suture had been carried out the wound began to heal, but broke down after 14 days, when an erythromycin-resistant staphylococcus was isolated from the wound; a similar strain was also isolated from the patient's nose. This patient had never before been in hospital or suffered from any staphylococcal infection. Moreover, he had never been treated with erythromycin and erythromycin was not being used in the ward at the time. Swabs were taken from the nose and open lesions of the other patients and attendants in the ward, and a staphylococcus with identical antibiotic sensitivities and phage pattern was isolated from swabs taken from the nose and from a leg ulcer of the patient in the next bed. This patient had previously been in a ward in another hospital where erythromycin had been used.

While it was possible that the first patient infected his own wound from his nose or skin, it was more likely that he acquired the erythromycin-resistant strain by cross-infection in hospital, since staphylococci with such a phage pattern and antibiotic sensitivity are not found among the non-hospital population. The source of infection was the patient with the leg ulcer, and it is pointed out that although the strain could be assumed to have originated in an erythromycin environment, it could be maintained and spread from one patient to another in an erythromycin-free environment. To limit the emergence and spread of erythromycin-resistant strains, it is recommended that patients under erythromycin treatment be nursed in isolation, and that a close watch should be kept for the appearance of resistant variants in patients and contacts. *R. B. Lucas*

28. **Pellagra Caused by Isoniazid**
R. J. HARRISON and M. FEIWEL. *British Medical Journal* [*Brit. med. J.*] **2**, 852–854, Oct. 13, 1956. 2 figs., 19 refs.

Infectious Diseases

29. **Puerperal Tetanus. Treatment with Muscle Relaxants and by Assisted Respiration**
A. M. Ramsay, E. M. France, and B. M. Dempsey. *Lancet* [*Lancet*] **2**, 548–550, Sept. 15, 1956. 15 refs.

The authors report, from the Royal Free Hospital, London, a moderately severe case of the rare condition of puerperal tetanus which occurred in a woman aged 33 who was admitted on the 6th day after a spontaneous abortion with clinical evidence of tetanus, the diagnosis being confirmed by positive bacteriological findings in a cervical swab and in uterine curettings. An intravenous injection of 200,000 units of tetanus antitoxin was given immediately, together with penicillin intramuscularly. Further treatment was based on establishing relaxation, for which a total dose of 8·6 g. of suxamethonium ("scoline") was administered over 7 days, and on maintaining an adequate airway, which was achieved initially by means of a cuffed endotracheal tube and then by a low tracheotomy, respiration being maintained manually for the first 3 days after which the patient was placed in a Beaver respirator for a further 8 days. Sedation was achieved by means of intravenous or intramuscular sodium amylobarbitone. Feeding was carried out through a gastric tube. The uterus was emptied of placental remnants at an early stage.

The course was complicated by the development of total collapse of the left lung, which was partly due to the aspiration of some granules of soda lime as a result of the breaking of the filter of the Waters canister. The patient was discharged home cured in 15 days. The authors have found that suxamethonium gives smoother control than tubocurarine. The treatment described above has greatly improved the prognosis in cases of tetanus. *John Fry*

30. **Treatment of Severe Tetanus with D-Tubocurarine Chloride and Intermittent Positive-pressure Respiration**
A. C. Smith, E. E. Hill, and J. A. Hopson. *Lancet* [*Lancet*] **2**, 550–552, Sept. 15, 1956. 1 fig., 11 refs.

The treatment of a boy aged 7 who developed very severe tetanus after receiving a cut on the forehead from a sharp stick fired as an arrow is reported from the Churchill Hospital, Oxford. There was an incubation period of 4 days. Very frequent and severe tetanic spasms occurred and were controlled by intermittent intravenous injections of curare through a Gordh needle, a total dose of 7,640 mg. being given over 26 days. Respiration was maintained through an elective lower tracheotomy by means of a Radcliffe respiration pump. Sedation was achieved with chloral hydrate, and antibiotics, with promethazine to minimize allergic effects, were administered; nutrition was maintained through a gastric tube and 2-hourly postural changes and physiotherapy were carried out to prevent chest complications. The boy made a complete recovery. *John Fry*

31. **Clinical Significance of Quantitative Enterokinase Determinations in the Faeces in Cases of Food Poisoning.** (Клиническое значение количественного определения энтерокиназы в кале больных пищевой токсикоинфекцией)
S. Y. Mikhlin, G. M. Kapnik, and O. N. Mukhina., *Терапевтический Архив* [*Ter. Arkh.*] **28**, 32–36, No. 3, 1956.

Whereas the enterokinase content of the faeces is normally less than 20 units per g., in acute food poisoning it ranges between 600 and 7,000 units per g., though there is no correlation with the severity of the illness. Persistence of a high faecal enterokinase content in such conditions as bacillary dysentery after clinical cure indicates residual infection and the need for further treatment. *R. Crawford*

INFECTIOUS DISEASES OF UNKNOWN AETIOLOGY

32. **Encephalomyelitis Simulating Poliomyelitis**
A. M. Ramsay and E. O'Sullivan. *Lancet* [*Lancet*] **1**, 761–764, May 26, 1956. 3 figs., 7 refs.

A description is given of 8 cases of acute encephalomyelitis seen between April and October, 1955, at the Royal Free Hospital, London, in patients aged 9 to 45 years, of whom 7 were female. The onset was generally insidious, with headache, limb pains, and giddiness as the more prominent symptoms, while lassitude, nuchal pain, upper respiratory tract infection with sore throat, vomiting, paraesthesiae, anorexia, and nausea were present in over half the cases. Muscular cramps, twitchings, pain referred to the ears, and tinnitus were also noted in some cases. On admission lymphadenopathy (chiefly of posterior cervical lymph nodes) was found in 7 cases, neck stiffness, paresis, and exaggerated reflexes in 6, objective sensory impairment and muscle tenderness in 5, cranial-nerve involvement in 4, extensor plantar responses in 3, nystagmus in 2, and diplopia in one. The accompanying pyrexia did not usually exceed 100° F. (37·8° C.).

The blood picture was characteristic of a virus infection, that is, there was neutropenia with occasional abnormal lymphocytes. The cerebrospinal fluid was normal in every case but one, in which the protein content reached 50 mg. per 100 ml. Culture of throat washings and/or faeces with monkey kidney tissue for Coxsackie and other viruses and serological tests of paired sera for lymphocytic choriomeningitis, mumps, leptospirosis, and all 3 types of poliomyelitis virus were negative in each case. Further, electromyography revealed no sign of the lower motor neurone degeneration characteristic of poliomyelitis, while the finding of long polyphasic units with reduced interference pattern

was characteristic of a myelopathic lesion. In 5 patients presenting behaviour changes the electroencephalogram (EEG) was abnormal, the abnormality being of a similar kind in all 5, with the presence of some bilateral activity in the range 4 to 7 c.p.s. and, in addition, slower episodic activity in 2 of these cases; the EEG changes were regarded as possibly non-specific. (Illustrative electromyograms and electroencephalograms are reproduced in the paper and brief clinical notes on each case are given.) Recovery was slow and convalescence protracted, mental and physical fatigue and emotional instability being present in half the cases. At follow-up 3 patients were still suffering from persistent weakness and sensory impairment 4 to 6 months after onset of the disease.

Joyce Wright

33. Further Outbreak of a Disease Resembling Poliomyelitis

D. W. SUMNER. *Lancet* [*Lancet*] **1**, 764–766, May 26, 1956. 9 refs.

The author describes a small explosive outbreak (7 cases) of a disease resembling poliomyelitis which occurred in November, 1954, and affected 6 young soldiers in one barrack block in Berlin and one orderly who nursed them. The incubation period was not more than 4 days. Characteristically the onset was with headache, followed in most cases by pains in the limbs and back and commonly by photophobia; pyrexia was mild. One representative case is described in detail, and the clinical findings in all 7 cases are summarized in a table.

Mental changes occurred in 3 of the patients and in some cases headache and depression persisted into convalescence. Blood examination showed a slight leucocytosis, with a normal differential count. The cerebrospinal fluid was normal in all but one case, in which 6 lymphocytes per c.mm. and a protein level of 86 mg. per 100 ml., with a moderate increase in the globulin fraction, were found. Agglutination tests against influenza A and B and for brucellosis and leptospirosis gave negative results; no cold agglutinins were found. Results of examination of the faeces for Coxsackie and poliomyelitis viruses were likewise negative.

Joyce Wright

34. Clinical Findings Six Years after Outbreak of Akureyri Disease

B. SIGURDSSON and K. R. GUDMUNDSSON. *Lancet* [*Lancet*] **1**, 766–767, May 26, 1956. 5 refs.

In 1948–9 an epidemic of 465 cases of a disease simulating poliomyelitis occurred in Akureyri, a town in Iceland, as previously reported (*Amer. J. Hyg.*, 1950, **52**, 222; *Abstracts of World Medicine*, 1951, **9**, 209). The authors now recall the clinical features of that outbreak, review reports of similar illnesses in other countries, and present the results in 33 female and 6 male patients affected in the 1948–9 epidemic who were re-examined neurologically in 1955. Only 12 of these showed no objective clinical signs of the illness and only 5 considered themselves completely recovered.

The residual signs and symptoms found in 1955 in all 39 patients are tabulated according to severity or mildness of the primary attack; taken together, they were as follows: nervousness and general tiredness (28 cases), weakness in one muscle group or limb (7), pain in muscles (24), paraesthesiae (4), sleeplessness (6), loss of memory (8), paresis (9), atrophy of muscles (6), reflex anomalies (5), tenderness of muscles (10), and hypoalgesia, hypoaesthesia, or dysaesthesia (8). Disturbances of cutaneous sensibility were slight, but in all such cases the distribution either followed the nerves or corresponded to spinal segments. Functional symptoms suffered by several patients in 1948–9 were still present in 1955.

Joyce Wright

35. Erythema Nodosum as a Manifestation of Sarcoidosis

D. G. JAMES, A. D. THOMSON, and A. WILLCOX. *Lancet* [*Lancet*] **2**, 218–221, Aug. 4, 1956. 7 figs., 7 refs.

The relationship between erythema nodosum and sarcoidosis was studied at the Middlesex Hospital, London, in a group of patients (7 men and 20 women, mostly young adults) suffering from the former condition. The Kveim test revealed the characteristic nodule of sarcoidosis in 19 cases, and sarcoid tissue was found on biopsy examination of erythematous lesions (2 cases), lymph nodes (4 cases), skin (5), and liver (4). In 24 of the 27 cases chest radiographs showed enlargement of the hilar lymph nodes; the lymphadenopathy was bilateral and symmetrical and the swelling persisted for an average of 6 months. In a few cases transient parenchymal mottling developed after the swelling of the nodes had subsided. No abnormality was found in the erythrocyte or leucocyte count, but there was a marked increase in the erythrocyte sedimentation rate.

Polyarthritis with pyrexia and sweating developed in 17 patients either before or during the attack of erythema. Acute rheumatism was diagnosed in 4 cases, but there was no evidence of cardiac damage or of abnormal antistreptolysin titres; furthermore, the response to salicylate therapy was poor. The results of the Mantoux test were of little assistance in determining the aetiology of the condition—since the test was not carried out before the illness it was impossible to decide whether conversion was of recent origin.

The authors emphasize the importance of histological examination in the differentiation of the sarcoidosis syndrome from erythema nodosum due to other causes; the prognosis is favourable in erythema nodosum associated with sarcoidosis.

A. Garland

36. Renal Insufficiency, Renal Calculi and Nephrocalcinosis in Sarcoidosis. Report of Eight Cases

D. A. SCHOLZ and F. R. KEATING. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 75–84, July, 1956. 1 fig., 14 refs.

Since 1940, 8 cases of sarcoidosis with renal complications have been seen at the Mayo Clinic, and in this paper the clinical manifestations and the problems in differential diagnosis are discussed. The patients were white males aged 28 to 74, and histological evidence of sarcoidosis was found in tissue specimens from lymph nodes in 6, skin in 1, and liver in 1. Renal calculi were

demonstrable in 5 cases, renal insufficiency in 2, and nephrocalcinosis in one case. The serum calcium level exceeded 10·5 mg. per 100 ml. in 6 instances. Significant hypercalciuria was found in 2 of the 3 patients in whom urinary excretion of calcium was studied. The serum concentration of inorganic phosphorus was abnormal in only one patient—5·4 mg. per 100 ml. in association with a grossly increased blood urea level. Albuminuria was present in all cases and haematuria was also noted in 5. Primary hyperparathyroidism was the initial diagnosis in 3 cases, and emphasis is laid on the difficulty of differentiating this condition from sarcoidosis with hypercalcaemia. Factors possibly responsible for the development of hypercalcaemia are discussed. The authors state that renal insufficiency may be secondary to widespread granulomatous infiltration, nephrocalcinosis, or a combination of both processes.

D. Geraint James

37. **Steroid Therapy of Hypercalcemia and Renal Insufficiency in Sarcoidosis**
R. W. PHILLIPS and D. P. FITZPATRICK. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1216–1222, June 28, 1956. 21 refs.

Attention is drawn to the value of cortisone in the treatment of hypercalcaemia and renal insufficiency due to sarcoidosis, and 2 illustrative cases seen at the Veterans Administration Hospital, Providence, Rhode Island, are described. After administration of cortisone by mouth for 14 days the serum calcium level, which had been very high, fell to normal and remained so, while laboratory investigations revealed gradual improvement in renal function. It is the authors' view that since hypercalcaemia in sarcoidosis can thus be quickly corrected, determination of the serum calcium level and the urinary excretion of calcium should be a routine procedure in all cases of this disease. If hypercalcaemia is present cortisone should be administered to prevent subsequent development of nephrocalcinosis.

D. Geraint James

VIRUS DISEASES

38. **An Epidemic Caused by a Virus of the A.P.C. Group.** (Eine durch das APC-Virus hervorgerufene Epidemie)
R. GLANDER, G. A. VON HARNACK, and H. LIPPELT. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 1147–1149, July 20, 1956. 6 refs.

The authors describe the combined experience of three Hamburg hospitals of an epidemic ascribed to infection with A.P.C. viruses which broke out in July, 1955, reached its maximum in September, and then gradually died out. Viruses of 6 serological types were isolated from 143 cases, one of which accounted for 92 cases, while another was found in only one case.

The clinical picture of the disease as it affected 55 children, 32 females and 23 males aged 1½ to 14 years, is described. The onset was acute with high fever which lasted 2 to 8 days and was remittent or intermittent in character. The most characteristic feature was the conjunctivitis which was seen in 47 cases (14 unilateral and 33 bilateral), the conjunctiva being bright red, oedematous, and granular. In over half the cases rhinitis, characterized by nasal obstruction rather than hypersecretion, occurred and enlargement of the tonsils and redness of the fauces were common. The tongue, covered with brown or white fur, resembled the "strawberry tongue" of scarlet fever. Enlargement of the lymph nodes was also common. In 18 cases the patient complained of pains in the trunk, while in 21 cases vomiting occurred. In 5 cases lumbar puncture showed the cerebrospinal fluid to be normal.

The blood count in 25 out of 53 proven cases showed a leucopenia with a granulocyte shift to the left; no eosinophilia was seen. The erythrocyte sedimentation rate ranged from 10 to 30 mm. in one hour. Treatment was symptomatic, antibiotics having no apparent effect.

I. M. Librach

39. **Report of an Epidemic Caused by a Virus of the A.P.C. Group.** (Bericht über eine durch das APC-Virus hervorgerufene Epidemie)
E. BRECKOFF. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 1149–1151, July 20, 1956. 2 refs.

The author describes his experience, as a general practitioner, of the epidemic ascribed to A.P.C.-virus infection which occurred in Hamburg from August to October, 1955. [See Abstract 38.]

A total of 241 cases were observed, all in patients below the age of 19, the maximum incidence being between 3 and 14 years. The social circumstances of the patients were mostly good. Of 1,500 school-children at risk, between 300 and 400 were affected and many school classes had to be closed.

The outbreak started during the first half of August, when many mild, short-lived, febrile illnesses occurred in the outskirts of the city. The diagnosis was at first uncertain, but the character of the illness in more severe cases which occurred later in the month suggested a viral origin, as did the resistance to sulphonamides and antibiotics. The incubation period was 4 to 5 days, the initial symptoms being severe headache and pains in the limbs. Many children complained of acute pain in the ears. Fever, which was high at first, lasted 4 to 5 days on average, falling by lysis. Clinically, there was faucial redness, enlargement of regional lymph nodes, stuffiness of the nose, and a heavily coated tongue, while conjunctivitis, bilateral in most cases, was a constant feature, conjunctival haemorrhage ranging in severity from petechiae to the confluent type seen in pertussis being common. No case of bronchitis, pleurisy, or pneumonia was seen, and cough was conspicuously absent. The liver and spleen were not enlarged. The leucocyte count in the acute stage ranged from 4,000 to 8,000 per c.mm., 60% of the cells being segmented polymorphonuclear granulocytes; eosinophils were present in all cases, though in reduced numbers. Treatment was entirely symptomatic.

The illness was generally more severe in the younger patients, although 3 infants showed nasal symptoms only.

Resistance seemed slow to develop, convalescence being protracted. Hospitalization was not necessary, however, and there were no deaths. *I. M. Librach*

40. **The Diagnostic Applications and Limitations of the Complement-fixation Reaction in Poliomyelitis.** (Diagnostische Anwendbarkeit und Grenzen der Komplementbindungsreaktion bei Poliomyelitis)
E. BERGER and M. VEST. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 776–778, July 7, 1956. 16 refs.

Complement-fixation tests were performed at the Children's Hospital, Basle, on sera from 98 cases of paralytic poliomyelitis, a micromethod, involving overnight fixation at 4° C., and antigens prepared commercially being used. A dose of 1·5 units of complement was employed. Fixation of complement at a serum dilution of 1 in 8 was regarded as positive. By this criterion serum from 85 cases gave a positive reaction, which in 18 was monospecific. In 54 cases more than one sample of serum was examined; of these, 24 were already positive by the 5th to 7th day of the illness, 22 were negative at that time but positive 7 to 9 days later, and 8, the maximum titre of which in the first sample had been 1 in 8, showed a twofold or greater rise in the second specimen.

The examination of sera from 103 cases of serous meningitis suspected to be due to poliomyelitis virus showed that 47 were positive, of which 11 gave monospecific reactions. In the 24 cases in which more than one sample of serum was examined, 11 were positive by the 5th to 7th day, 10 were negative at that time but positive 7 to 9 days later, and 3 showed a twofold or greater rise in titre from the maximum value of 1 in 8 found in the first sample. Of the sera from 45 cases of miscellaneous febrile illnesses which were not suspected of being due to poliomyelitis virus, 6 gave a positive result, while of those from 27 cases of afebrile illness, 2 yielded a positive result. In a lengthy discussion the authors point out the rapidity and relative simplicity of the test compared with other laboratory methods for the diagnosis of poliomyelitis, but admit that its lack of specificity has certain disadvantages.

J. E. M. Whitehead

41. **The Treatment and Prophylaxis of Poliomyelitis.** (Основные вопросы клиники, лечения и профилактики полиомиэлита)
M. B. TSUKER. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 24–30, No. 6, June, 1956. 1 ref.

The author describes in detail three clinical forms of poliomyelitis, which he describes as (1) abortive, (2) non-paralytic, and (3) paralytic. In discussing the differentiation of Types 2 and 3 he singles out electromyography as a useful means of detecting slight affections of the peripheral motor neurones. The paralytic type is subdivided into (*a*) spinal, (*b*) bulbar, (*c*) pontine, and (*d*) encephalitic, meningeal, and polyneuritic forms, though it is pointed out that mixed forms are very common. In all types of case the cardiovascular and respiratory systems may be affected. Hypertension is quite common, and functional disorders of the heart are stated to occur in 10 to 20% of cases.

In addition to the usual treatment, the author suggests that penicillin and streptomycin should be given whenever there are changes in the respiratory tract. The administration of ascorbic acid in large doses is regarded as very important, while glucose and vitamin B_{12} are recommended by some authorities. To increase the metabolism of nervous tissues the administration of amino-acids, and especially glutaminic acid or its magnesium salt, is essential.

The dissemination of the virus by undiagnosed cases and by carriers is discussed. According to Melnik the number of carriers in any region in which infection by sewage is likely is 50 to 70 per 1,000 population, and the number of persons actually affected 0·13 per 1,000. Since the virus is excreted in the faeces, sewage is an important factor in dissemination, while flies also may carry the infection. The virus has been isolated from vegetables grown in kitchen gardens which have been fertilized with infected sewage. *H. W. Swann*

42. **Maintenance of Respiratory Function in Poliomyelitis and Other Neuromuscular Disorders**
W. H. KELLEHER, J. M. MEDLOCK, and D. G. B. POWELL. *Lancet* [*Lancet*] **2**, 68–74, July 14, 1956. 2 figs., 7 refs.

Experience in the treatment of respiratory palsy by various methods at the Western Hospital, London, is reported. Between December, 1954, and January, 1956, a total of 70 patients were admitted to the poliomyelitis unit of the hospital, including 63 with acute anterior poliomyelitis (spinal (respiratory) in 39, bulbar in 2, and bulbo-spinal in 22), 5 with toxic polyneuritis (bulbar paresis in 2), and 2 with encephalomyelitis. The authors emphasize that early recognition of ventilatory insufficiency is important, and determination of blood pressure, vital capacity, and the patient's ability to count aloud in one expiration are helpful. Treatment depended on the presence or absence of lung damage (congestion or collapse), excess mucus, or difficulty in swallowing. The standard cabinet (tank) respirator, adapted to give better access for nursing and physiotherapy, proved an efficient machine for cases of simple paralysis of the respiratory muscles; in the presence of congestion or collapse of the lungs frequent change of position and active chest physiotherapy were needed. For the management of cases in which there was also excessive mucus the authors chose either tracheotomy and the cabinet respirator or intermittent positive-pressure respiration (I.P.P.R.) through a cuffed tracheotomy tube. Where lung damage with accumulation of mucus was associated with difficulty in swallowing, tracheotomy with a cuffed tube and either the cabinet respirator or I.P.P.R. gave the best results. For bulbar palsy alone postural drainage with tube feeding was the treatment of choice. The methods of prevention and treatment of lung complications are discussed, as are the difficulties which may be encountered when artificial respiration is withdrawn.

[This paper merits further study.]

G. C. R. Morris

Tuberculosis

43. **Prophylaxis of Isoniazid Neuropathy with Pyridoxine**
H. B. CARLSON, E. M. ANTHONY, W. F. RUSSELL, and G. MIDDLEBROOK. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 118–122, July 19, 1956. 17 refs.

An investigation is reported from the National Jewish Hospital and the University of Colorado School of Medicine, Denver, of the effects of prophylactic administration of pyridoxine (25 to 200 mg. daily) to 274 patients receiving a daily dosage of 8 mg. or more of isoniazid per kg. body weight for at least two months. Only 11 of these complained of symptoms suggestive of isoniazid toxicity, chiefly paraesthesiae and numbness in the hands and feet without demonstrable neurological defect. When the dosage of pyridoxine was increased 8 were able to tolerate further isoniazid therapy. Side-effects precluded continued administration of isoniazid to 2 patients, in one of whom a severe anxiety neurosis developed and in the other optic neuritis. It was found that 25 mg. of pyridoxine prevented significant peripheral neuropathy in most patients receiving 8 mg. of isoniazid per kg. body weight daily, and 50 mg. of pyridoxine was adequate for those receiving 16 mg. of isoniazid per kg. daily.

I. Ansell

DIAGNOSIS AND PROPHYLAXIS

44. **British Freeze Dried BCG Vaccine: Preliminary Clinical Trial**
J. LORBER, C. B. L. HART, P. FARMER, and P. W. MUGGLETON. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 187–194, June, 1956. 22 refs.

Since 1949 a Danish liquid B.C.G. vaccine has been widely used in Great Britain, and although generally satisfactory, such liquid suspensions have certain disadvantages, which are discussed. The authors then report the results of a clinical trial, carried out at the University of Sheffield, of a British freeze-dried B.C.G. vaccine. The primary objects of the trial were: (1) to ascertain the number of viable organisms required to cause satisfactory conversion of the tuberculin reaction in a vaccinated patient; (2) to establish the keeping properties of the vaccine during prolonged periods at room temperature; and (3) to compare the local lesions with those produced by fresh Danish vaccine and to establish the duration of allergy and presumed immunity after vaccination.

During a period of 12 weeks 276 newborn infants were vaccinated in the first 8 days of life with one or other of two batches of the new vaccine under carefully controlled conditions. After 6 weeks the local lesion was inspected and a tuberculin jelly test was carried out; if the result of this proved negative a Mantoux test with 1 in 1,000 old tuberculin was carried out. This procedure was repeated at 12 weeks in all infants giving a negative reaction to the first test or who had escaped it. Viable cell counts were also carried out on the vaccines weekly during the period of the trial and at 10 or 12 months after manufacture, while sensitization tests on guinea-pigs were performed at intervals up to 3 months after the date of manufacture. To provide a control series the results were compared with those in 106 newborn infants given the Danish liquid vaccine during the previous 2 years.

From the results obtained, which are presented in tables, the following conclusions are drawn. (1) The low viability of the vaccine did not cause any untoward reactions, and the local lesions were much smaller and milder than those produced by the liquid vaccine. (2) There was a delay in tuberculin conversion with the freeze-dried vaccine; thus, at 6 weeks after vaccination 80% of the babies were tuberculin-positive and at 12 weeks 94%, whereas 105 out of the 106 children given the liquid vaccine were tuberculin-positive at 6 weeks. (3) Neither batch of the vaccine showed any deterioration in antigenic properties during the period of the trial nor, as judged by the guinea-pig tests, up to 3 months after manufacture. Viable cell counts at 40 to 52 weeks after manufacture showed a slight but insignificant diminution in viability.

The authors conclude that for mass vaccination the potential advantages of freeze-dried B.C.G. vaccine are considerable, but as the number of viable organisms present in the batches tested was just below the number required to produce 100% conversion in a short period they would not be suitable for vaccination of contacts.

John M. Talbot

45. **Freeze-dried B.C.G. Vaccine. Methods Adopted in Preparation of a Standard Product**
J. UNGAR, P. FARMER, and P. W. MUGGLETON. *British Medical Journal* [*Brit. med. J.*] **2**, 568–571, Sept. 8, 1956. 10 refs.

A method is described for the production of a freeze-dried B.C.G. vaccine by using dextran with glucose as a protein-free drying medium. The B.C.G. organisms for vaccine production can conveniently be grown in deep culture in Sauton's medium with 0·025% triton WR 1339—a non-ionic polyoxyethylene ether—without affecting their biological properties. The bacteria, uniformly dispersed, can be easily harvested in the centrifuge and the deposit resuspended in dextran–glucose solution.

A method is described for enumerating the viable cells with consistent results; the viable-cell content of different batches of vaccine can be accurately standardized. A study of the keeping properties of the dried vaccine has shown that it has a life of at least 12 months when stored below 20° C. The relationship between the viable-cell counts of various batches and the tuberculin

conversion of guinea-pigs is shown. There is also a direct correlation between the viable-cell count and the size of local lesions in guinea-pigs after intradermal injection.—[Authors' summary.]

46. **Serum Gamma Globulin in Childhood Tuberculosis**
C. M. ZITRIN, E. M. LINCOLN, A. SAIFER, and S. LEWKOWICZ. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **74**, 15–28, July, 1956. 4 figs., 21 refs.

Using a simplified chemical test in place of electrophoresis, the authors studied the serum gamma-globulin level at the Bellevue Hospital Center, New York, in 18 children with various forms of tuberculosis. They confirmed Siebert's findings (*J. clin. Invest.*, 1947, **26**, 90) that the level is raised in active tuberculosis. Serial determinations showed that in children with a low serum gamma-globulin level initially (presumably due to inefficient antibody formation) the prognosis is poor unless there is a subsequent rise. In children in whom the serum gamma-globulin level is raised initially improvement in the clinical condition is accompanied by a return to normal values.

The authors consider that children with low serum gamma-globulin levels should receive more intensive antituberculous therapy, possibly with the addition of large doses of gamma globulin, as given in cases of agammaglobulinaemia. *Wilfrid Gaisford*

RESPIRATORY TUBERCULOSIS

47. **The Tuberculous Infectivity of Progressive Massive Fibrosis**
R. G. CARPENTER, A. L. COCHRANE, W. E. MIALL, T. F. JARMAN, and G. HOCKADAY. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 225–232, Aug., 1956. 3 figs., 10 refs.

This paper reports the results of further analysis of the data obtained in the two surveys carried out by the Pneumoconiosis Research Unit of the Medical Research Council in the Rhondda Fach, South Wales, in 1950–1 and 1953. Figures are given for the prevalence of sputum positive for tubercle bacilli among miners with progressive massive fibrosis (P.M.F.), " the attack rate of positive sputum " (that is, the rate at which tubercle bacilli appeared in the sputum of these men), and the case fatality rate. Children living in the same households as men with P.M.F. and negative sputum were Mantoux tested and the results compared with those in children from control households. There appeared to be no difference in the number of positive reactors in these two groups. In a discussion of the importance of cases of P.M.F. as possible reservoirs of tuberculous infection the necessity for repeated sputum examination rather than *x*-ray examination is stressed.

P. Mestitz

48. **Respiratory Function before and after Plombage**
R. L. HURT. *Tubercle* [*Tubercle* (*Lond.*)] **37**, 341–346, Oct., 1956. 1 fig., 31 refs.

49. **The Contribution of Pituitary Somatotrophic Hormone to the Treatment of Pulmonary Tuberculosis.** (L'apport de l'hormone somatotrope hypophysaire dans le traitement de la tuberculose pulmonaire)
J. GUILLERMAND, G. DUCHÉ, and J. FALCOZ. *Thérapie* [*Thérapie*] **11**, 637–645, 1956. 4 figs., 20 refs.

The authors report their results in 40 patients with pulmonary tuberculosis who were treated at the Military Hospital, Grenoble, with pituitary somatotrophic hormone, 7 receiving the hormone alone and 33 with antituberculous drugs, generally isoniazid in doses of 300 mg. daily and streptomycin in doses of 2 g. weekly. The dose of the hormone was 100 rat units daily for 20 days.

The best results were obtained in cases showing cavitation. Thus of 13 patients with recent cavities, the cavity closed in 4, diminished in size in 3, showed a perifocal reaction in 2, and was unchanged in 4. Of 13 with a more chronic cavity, this closed in one case, diminished in size in 8, showed perifocal reaction in 2, and was unchanged in 2. There was also some improvement in patients with non-cavitary disease and in 3 cases of pyothorax; in the latter there was diminution in the size of the pleural pocket and closure of the fistula, the closure, however, being only temporary in 2 cases. Electrophoretic studies of the serum proteins showed a decrease in the albumin and an increase in the globulin content, particularly in the γ-globulin fraction. The tuberculin reaction was increased in 17 out of 23 patients tested at the end of treatment.

It is considered that in the future pituitary somatotrophic hormone will occupy an important place in the treatment of tuberculosis, in which its action is the opposite of that of ACTH or cortisone.

G. M. Little

50. **The Indications for Hydrocortisone and Prednisone in the Treatment of Active Pulmonary Tuberculosis.** (Les indications de l'hydrocortisone et de la prednisone dans le traitement de la tuberculose pulmonaire évolutive)
G. FAVEZ and F. AGUET. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **86**, 843–851, July 28, 1956. 36 figs., bibliography.

The demonstration of the anti-inflammatory properties of the adrenocorticoids has led the authors to combine hydrocortisone and prednisone with streptomycin, PAS, and isoniazid in the treatment of active and progressive pulmonary tuberculosis, and the present paper gives brief details in tabular form, accompanied by reproductions of radiographs, of 40 such cases which were treated at the University Medical Clinic, Lausanne.

There were 31 men and 9 women in the series, and their ages ranged from 16 to 76. In 12 cases the disease was of long standing, and in the remaining 28 it was of recent onset or had become reactivated after a period of quiescence, the lesions being exudative and infiltrative in type, with cavitation in 11 cases. Three cases were complicated by tuberculous laryngitis, one by pleurisy, and 2 by tuberculous meningitis (together with renal tuberculosis in one case). Five patients with chronic and 8 with recent disease had had a previous course of chemotherapy varying in duration from 10 days to

3 months, during which 6 of the recent cases had deteriorated, one developing a spontaneous pneumothorax.

The combined regimen was continued for one month, 100 mg. of hydrocortisone, 500 mg. of isoniazid, and 2 g. of streptomycin being given daily. Thereafter the dose of streptomycin was reduced gradually to 1 g. 3 times weekly, with 18·5 g. of PAS intravenously 6 days weekly. In spite of the high dosage of streptomycin the authors noted only occasional and temporary vestibular disturbances, but the usual side-effects of cortisone were observed in several cases.

No further haematogenous spread was observed in any of the patients. All those with disease of recent onset, including those with tuberculous meningitis and laryngitis, improved both clinically and radiologically during the period of combined therapy, though 7 still had a positive sputum at the end of the period of observation (2 to 6 months).

In the long-standing cases further spread appeared to be arrested, but there was little change in old cavities and fibrotic lesions. The sputum was still positive at the conclusion of treatment in 8 cases. A further series of 30 patients with pulmonary tuberculosis with recent spread were treated similarly, but prednisone (25 mg. daily) was substituted for hydrocortisone. These cases, which are not described in detail, are stated to have responded in a comparable manner, but the side-effects were no less marked than with hydrocortisone.

H. F. Reichenfeld

51. **Prolonged Chemotherapy in Chronic Pulmonary Tuberculosis with Combinations of Isoniazid, *para*Aminosalicylic Acid, and Streptomycin**

C. L. Joiner, K. S. Maclean, K. Marsh, J. D. Carroll, and R. Knox. *Lancet* [*Lancet*] **2**, 165–169, July 28, 1956. 7 refs.

In a previous paper (*Lancet*, 1954, **2**, 663; *Abstracts of World Medicine*, 1955, **17**, 103) the authors reported that the incidence of drug resistance in a group of 13 patients with chronic pulmonary tuberculosis who received the three drugs streptomycin, PAS, and isoniazid in pairs in rotation (Group R) was less than that in a comparable group (Group IP) of 14 patients receiving a prolonged course of PAS and isoniazid only, and that after 24 weeks the former showed greater clinical improvement. The treatment of both groups has now been continued for 2 years, and this article records the results obtained up to this point. The dosage of isoniazid was 250 mg. and of PAS 10 g. daily in both groups, and that of streptomycin in Group R 1 g. intramuscularly twice a week. In the latter group each of the 3 pairs was given for 4 weeks at a time, the cycle being repeated at the end of 12 weeks. Treatment was contained until the sputum, examined every 2 weeks, had been negative for tubercle bacilli for 36 weeks, and was restarted in the event of relapse. Four patients (in Group IP) left the trial before 2 years' treatment was completed, being too ill to continue treatment as out-patients, and one patient in each group died—one of cerebral thrombosis and the other of cor pulmonale.

Sputum conversion was successful in all 12 surviving patients in Group R and in only 5 of the 9 in Group IP, a difference that is statistically significant. Of the 4 in Group IP whose sputum remains positive, 3 relapsed after treatment had been stopped. Throughout the period of observation the erythrocyte sedimentation rate in Group IP was higher, on average, than in Group R, the average reading for the 5 sputum-negative cases in the former at the end of the 2-year period being 33 mm. in one hour compared with 14 mm. in the latter. Whereas even those patients in Group IP whose treatment was successful gained no weight, those in Group R gained an average of 6 lb. (2·7 kg.). Similarly, all the patients in Group R showed radiological improvement at the time of stopping treatment, whereas only 7 of those in Group IP showed improvement at that time or when last examined. The authors suggest that the greater success of treatment in Group R may be attributed largely to the avoidance of drug resistance, which developed in all but one of the cases of failure in Group IP. At the same time, however, they point out that other factors, unconnected with the treatment regimen, may have contributed—for example, the greater average weight, resulting in a lower concentration of drugs in the tissues, of the patients in Group IP who did not respond compared with that of the rest of their group and that of the other group. Previous treatment also may have had some deleterious effect, since of 7 patients in Group IP who had had "significant" treatment with PAS in the past (2 months with PAS alone, or 4 months in combination with another drug), only in one was treatment in the present trial a success. However, in 4 out of 5 cases in Group R previous PAS treatment did not prevent success. No conclusion could be reached concerning the effect of previous treatment with streptomycin or isoniazid.

In view of their results the authors advise that the three antituberculous drugs be given in rotation in the treatment of chronic pulmonary tuberculosis (no conclusions being reached concerning the treatment of acute cases). They also emphasize the need for prolonged treatment—in 2 of their cases the sputum remained positive for 52 weeks before becoming negative.

Arthur Willcox

52. **Treatment of Pulmonary Tuberculosis on a Combined Regimen of *para*-Aminosalicylic Acid, Streptomycin and *iso*Nicotinic Acid Hydrazide**

T. Kumagai, S. Oka, C. Suzuki, T. Kurobane, I. Kanno, S. Sato, Y. Niitu, S. Awataguchi, H. Ueda, S. Yamada, E. Yakuwa, T. Sugawara, M. Shoji, A. Kanaya, and K. Komatsuda. *Reports of the Research Institute for Tuberculosis and Leprosy, Tohoku University* [*Rep. res. Inst. Tuberc. Lepr. Tohoku Univ.*] **6**, 401–432, March, 1956 [received July, 1956]. 28 refs.

The study here reported from Tohoku University, Sendai, Japan, was carried out on a group of 336 patients with pulmonary tuberculosis who received combined treatment with PAS, streptomycin, and isoniazid for periods ranging from 4 to 24 months. The dose of PAS was 10 g. daily, and of streptomycin 0·5 to 1 g. and isoniazid 3 to 4 mg. per kg. body weight twice weekly; 233 patients had previously received chemotherapy, 122

were sputum-negative, and cavities were visible radiologically in 238 cases.

The authors were most impressed with the results. The sputum conversion rate in cases in which a smear was positive initially was 90%, and in cases in which the sputum was positive only on culture it was 100%. The *x*-ray appearances improved in 82·7% of cases. The incidence of drug resistance was low and the results were equally good in those patients who had had previous chemotherapy. The authors were also of the opinion that bacillary resistance, when it developed, tended to regress as the treatment continued. They recommend that treatment should be continued for at least 1½ year, but they are of the opinion that isoniazid may induce haemoptysis and that this drug should be suspended if this complication occurs. *Paul B. Woolley*

53. **Are Chemotherapy and Collapse Therapy for Pulmonary Tuberculosis Compatible? II. A Study in Cavities in the Upper Lobe**
T. KUMAGAI, C. SUZUKI, S. OKA, T. KUROBANE, I. KANNO, S. SATO, S. AWATAGUCHI, Y. NIITU, E. YAKUWA, and H. ABE. *Reports of the Research Institute for Tuberculosis and Leprosy, Tohoku University* [*Rep. res. Inst. Tuberc. Lepr. Tohoku Univ.*] **6**, 433–459, March, 1956. 19 figs., 9 refs.

In a previous report (*Rep. res. Inst. Tuberc. Lepr. Tohoku Univ.*, 1955, **6**, 133; *Abstracts of World Medicine*, 1956, **19**, 197) the authors compared the results of different methods of treatment in 111 cases of tuberculosis of the lower lobes and concluded that chemotherapy and collapse measures in such cases were incompatible. The present study deals with an investigation of 212 patients with upper-lobe cavities who were treated with various combinations of chemotherapeutic agents, with and without the addition of artificial pneumothorax or pneumoperitoneum.

Whereas pneumothorax improved the results of chemotherapy only in respect of PAS given alone and was responsible for various complications, the addition of pneumoperitoneum to combined treatment with PAS, streptomycin, and isoniazid helped to reduce the size of cavities, especially when these were large, although the rate of closure was not significantly increased. Theories concerning the action of antituberculous drugs and their effect on the mechanism of cavity closure when used concurrently with collapse therapy are discussed at some length. *Paul B. Woolley*

54. **Segmental and Fractional Resection of the Lung for Tuberculosis.** (Сегментэктомия и частичные экономные резекции легкого при туберкулезе)
I. S. KOLESNIKOV. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 9–16, No. 3, May–June, 1956 [received Sept., 1956].

In the period 1948–52, at the Surgical Clinic of the Institute of Tuberculosis, Kirov, lung resection operations comprised 30 pneumonectomies and 4 lobectomies; in 1953 there were 13 pneumonectomies and 17 lobectomies; in 1954, 24 patients were treated by pneumonectomy, 86 by lobectomy, 6 by segmental resection, and 17 by fractional resection, while in 1955 the corresponding figures were 58, 134, 29, and 11 respectively. The postoperative mortality, including that from postoperative complications (up to 1½ year in some cases) was 23·5% for the period 1948–52, 13·3% for 1953, 9% for 1954, and 8·2% for 1955. The operative mortality for pneumonectomy was 14·3% and for the lesser types of resection 5·5 to 5·7%.

In the author's experience the indications for segmentectomy are: (1) the presence of blocked cavities in one or two segments, provided the rest of the lung is in relatively good condition; (2) cavities in atelectatic zones; (3) discrete, coarse, caseous foci, particularly if situated in Segments 1 and 2 of the upper lobe or Segment 6 of the lower; (4) cavities with thick walls; and (5) cavities remaining patent after performance of one or other collapse procedure. Surgical excision may also be considered for fresh cases which fail to respond to 6 to 12 months' conservative treatment. The author considers that with improvement in the technique and results of segmental resection other operations (such as extrapleural pneumothorax or cavernotomy) will be practised less frequently, and probably mainly when resection is impossible. The segmentectomy technique employed is described. *R. Crawford*

55. **The Surgical Treatment of Patients with Late Progressive Pulmonary Tuberculosis Recurring after Resection.** (Хирургическое лечение больных с поздним прогрессированием туберкулеза после резекции легкого)
N. M. AMOSOV. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 22–27, No. 3, May–June, 1956.

Writing from the Ukrainian Institute of Tuberculosis the author reports that up to December, 1954, there had been 26 cases of recurrence of pulmonary tuberculosis among 300 patients subjected to lung resection—21 among 120 patients operated on at Bryansk in the period 1950–2 and 5 among 180 treated at Kiev in the period 1952–4, the higher incidence at Bryansk being ascribed not only to the longer interval but also to the unfavourable conditions prevailing there, such as non-availability of tomography, limited supplies of streptomycin, no sanatorium treatment, and adverse housing conditions. The recurrence rate was 6·4% in the first year after operation, 3·2% in the second year, and 0·8% in the third. There were fewer recurrences after pneumonectomy (9 among 188 cases) than after lobectomy and fractional excisions (16 among 112). Recurrence took place in 5 out of 106 cases with multiple cavities (94 treated by pneumonectomy and 12 by lobectomy) and in 10 out of 70 cases with a cavity confined to one lobe.

Recurrences were generally insidious and were not accompanied by marked deterioration in the general condition. Despite systematic examination the infiltration changes preceding cavity formation were not detected in any of the cases, and it is thought that the changes in intrapleural pressure resulting from operation may determine the rapid conversion of small cavities to large ones. While prevention of recurrence is important, it is impossible to limit excision to strictly unilateral

cases; excision in bilateral cases is combined with the administration of antibiotics before and after operation and with sanatorium treatment. Since after resection the vital capacity and other respiratory indices frequently return almost to normal levels, further intervention (such as excision and the induction of extrapleural or intrapleural pneumothorax) is possible in recurrent cases; 15 such operations are reported, but were too recent to allow of adequate appraisal. *R. Crawford*

56. **Results of Lung Resection in Tuberculosis.** (Результаты резекции легких при туберкулезе)
Z. I. KISELEVA. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 27–30, No. 3, May–June, 1956.

Between June, 1950, and August, 1952, pneumonectomy was performed at Bryansk Tuberculosis Clinic on 49 patients and partial lung resection on 54 for the treatment of cavernous forms of pulmonary tuberculosis, with 3 postoperative deaths. In October, 1954 (after periods of observation ranging from 2¼ to 4½ years) 63 of the patients were regarded as showing good clinical results, 14 had late sequelae (bronchial or thoracic fistulae and recurrence of empyema), and in 23 the disease process had recurred in the remaining part of the same lung or in the opposite lung. Of the 69 workers in the group (the remainder were housewives or students) 82·6% were capable of work and 65·2% had actually returned to work. *R. Crawford*

57 (*a*). **The Treated Pulmonary Lesion and Its Tubercle Bacillus. I. Pathology and Pathogenesis**
W. E. LORING and H. VANDIVIERE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 20–29, July, 1956. 7 figs., 35 refs.

57 (*b*). **The Treated Pulmonary Lesion and Its Tubercle Bacillus. II. The Death and Resurrection**
H. M. VANDIVIERE, W. E. LORING, I. MELVIN, and S. WILLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 30–37, July, 1956. 3 figs., 16 refs.

In the first of these two papers the microscopical appearances of treated tuberculous lesions in surgical specimens of lung tissue are described, and an attempt is made to distinguish between the changes produced by streptomycin therapy and those produced by isoniazid. The lethal effect of the latter drug on the organisms is correlated with modifications in the classic histological picture of pulmonary tuberculosis, and further evidence of the open healing of cavities is presented.

In the second paper the authors discuss the effects of treatment on the viability and metabolic activity of tubercle bacilli in resected lesions. In a bacteriological investigation of specimens of tissue from 84 patients incubation of cultures for 6 to 18 months instead of the usual 8-week period increased significantly the number of positive cultures obtained. Viable, resistant organisms were almost constantly present in unhealed open cavities and absent from all healed end-stage cavities. Such organisms were isolated from 9 of 22 closed cavities, but only on extended incubation. Very few solid lesions yielded positive cultures even on extended incubation.

[Unfortunately, the dosage schemes used and the total amounts of the drugs administered to these patients are not stated.] *P. Mestitz*

TUBERCULOUS MENINGITIS

58. **Observations on the Treatment of Tuberculous Meningitis with Saluzid.** (Наблюдения по лечению туберкулезного менингита салюзидом)
A. L. BERNSHTEĬN, R. B. KRASIL'SHCHIK, and A. A. SHELAGUROVA. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **34**, 55–60, No. 7, July, 1956.

" Saluzid ", which has been synthesized in the U.S.S.R., belongs to the group of hydrazine derivatives of *iso*-nicotinic acid. The present report describes its use in the treatment of 55 patients with tuberculous meningitis at the First City Infectious Diseases Hospital, Moscow, of whom 19 were children, 13 adolescents, and 23 adults. The first 10 patients were treated with saluzid only, doses of 26 to 58 mg. per kg. body weight daily being given orally and 2 to 3·9 mg. per kg. daily in a 5% solution intrathecally.

Of 6 of these patients who had recurrent tuberculous meningitis, 4 improved satisfactorily with saluzid alone; the other 4 patients had acute tuberculous meningitis and although they improved initially with treatment, their condition worsened again later and the treatment was abandoned after 13 to 35 days, in favour of intramuscular and intrathecal streptomycin, with oral " phthivazid " [a derivative of isoniazid].

In the treatment of the subsequent 45 cases saluzid was given after or in combination with streptomycin as follows. (1) Of 15 patients to whom saluzid alone was given orally and intrathecally after a course of streptomycin, satisfactory results were obtained in all, though the infection recurred in 2 cases. (2) Of 11 patients, all of whom had severe meningitis with recurrences and complications and who already had received prolonged courses of streptomycin, PAS, and phthivazid, 9 were sufficiently improved following treatment with saluzid to be discharged, although all suffered from some residual damage. (3) Five patients were given saluzid orally together with streptomycin intramuscularly and intrathecally; this group was too small to allow of any useful evaluation of the method or to indicate whether saluzid was any more effective than phthivazid used previously. (4) In this group 14 patients were treated with intramuscular streptomycin, oral saluzid, and alternating daily intrathecal injections of streptomycin and saluzid. In these patients the clinical improvement was rapid and satisfactory, and there were no toxic side-effects. Although the permanence of the clinical results could not be assessed with certainty, the authors felt that this combination offered the most effective therapy and was better than a combination of streptomycin, phthivazid, and PAS. They stress that saluzid did not cause any toxic reactions even after administration for up to 240 days in doses of as much as 3·6 mg. per kg. body weight per 24 hours intrathecally and 64 mg. per kg. per 24 hours orally. *Marcel Malden*

Venereal Diseases

59. **Immunity in Experimental Syphilis. The Concept of Cellular Refusal.** (A propos de l'immunité dans la syphilis expérimentale. La notion de refus cellulaire)
P. GASTINEL, P. COLLART, and A. VAISMAN. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **90**, 677–687, June, 1956. 25 refs.

From previous experiments carried out at the Institut Alfred-Fournier, Paris, on immunity in rabbits infected with the Nichols strain of *Treponema pallidum* the authors concluded that resistance to reinfection is not due to any germicidal activity in the host's tissues, since the strain remained virulent for fresh rabbits for at least 8 to 10 days. In the further experiments now described serial examinations of tissue from inoculated immune rabbits failed to show any inflammatory or phagocytic reaction around the inoculum. It is postulated that there exists a state of "cellular refusal" in which a previously infected organism refuses to accept further amounts of the infecting agent. This type of "cellular memory" is thought to be a fundamental element in immunology. *G. W. Csonka*

60. **The Detection of Syphilitic Reagin by Means of the Conglutination Reaction.** (Recherche de la réagine syphilitique à l'aide de la réaction de conglutination)
M. FAURE and F. DAOULAS-LE-BOURDELLLÈS. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **90**, 763–769, June, 1956. 7 refs.

In this communication from the Institut Pasteur, Paris, the technique of the conglutination reaction is fully described [and should be read in the original, as it does not lend itself to abstracting]. In a comparative study the techniques of Kline and Kolmer and the conglutination reaction were used to detect syphilitic reagin in 87 syphilitic and 274 presumably non-syphilitic sera. Only in 3 of the 274 controls was the negative reaction in doubt. With the conglutination test the syphilitic sera gave reactions 2 to 8 times as sensitive as those obtained with the Kolmer test; zoning, however, was frequently encountered, and for this reason the reaction should not be used for routine diagnostic purposes, though its high sensitivity may be useful in difficult cases. *G. W. Csonka*

61. **TPI Test as a Daily Routine Laboratory Procedure**
A. HARRIS. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **46**, 723–727, June, 1956. 12 refs.

The results obtained during a 9-month period with the treponemal immobilization (T.P.I.) test which, with certain modifications, is in daily use at the Venereal Disease Research Laboratory, Chamblee, Georgia, are evaluated. Of 1,851 specimens of serum submitted to the laboratory for examination, 126 were unfit for testing; of the remainder, 742 (43%) gave a positive reaction, 26 (1·5%) a weakly positive reaction, 940 (54·5%) a negative reaction, and only 17 (1%) gave an inconclusive result. Detailed information regarding the clinical diagnosis was available in respect of 1,700 sera; of these, 205 were from patients believed to have syphilis, 1,267 were thought to have given a false positive reaction, and no opinion was stated in respect of 228. Thus approximately 75% of the patients were considered to be false positive reactors, and of these 1,267 specimens of serum, 506 gave a positive reaction to the test. Of 98 specimens from patients with a previous history of syphilis, 26 were negative by the T.P.I. test. Of the 205 cases of suspected syphilis a history of syphilis was obtained in 96, and in 75 of these the result of the T.P.I. test was positive; of the 109 cases with no such history, only 64 gave a positive reaction.

It is concluded that in all three categories studied the serum of patients with a history of past syphilitic infection produced a greater percentage of positive findings by the T.P.I. test (75%) than did those without such a previous history (42·5%). Approximately one-third (32·2%) of the sera from patients regarded as having syphilis failed to react to the T.P.I. test. In the biological false positive category a 60% agreement with the T.P.I. test results was obtained. The over-all agreement between the clinical diagnosis and the T.P.I. test result was approximately 60%. *R. R. Willcox*

62. **The Value of the Nelson Test in the Diagnosis of Congenital Syphilis in Early Infancy.** (L'intérêt du test de Nelson pour le diagnostic de la syphilis congénitale dans la première enfance)
G. ROMAGNY. *Pédiatrie* [*Pédiatrie*] **11**, 419–437, 1956.

The author throws some doubt on the absolute reliability of the treponemal immobilization (T.P.I.) test of Nelson in the diagnosis of congenital syphilis, and quotes 29 case histories, some of which seem to suggest that the T.P.I. test may occasionally give false results. Clinicians are familiar with the difficulties in children in the interpretation of routine standard tests for syphilis (S.T.S.), in which the greatest difficulty is experienced in the interpretation of "doubtful" reactions. The author regards the T.P.I. test as another laboratory test, more sensitive than the S.T.S., but with definite limitations, its greatest value being as an instrument of research into the transmission of congenital syphilis.

He suggests that treatment, while otherwise successful, may have allowed the persistence of scarcely recognizable forms of abortive congenital syphilis. In doubtful cases, and in cases in which there are inexplicable variations in titre, interpretation may be possible only by long observation and repetition of the tests. The duration of persistence of antibody transmitted to the child is not known, nor is the significance of positive reactions

persisting after treatment, although it has been customary to accept a limit of 3 months for a positive S.T.S. reaction due to transmitted antibodies. In this field the T.P.I. test has not replaced the earlier routine tests.

Robert Lees

63. **Serological Examinations of Electrophoretically Separated Serum Components with Cardiolipin Antigen and an "Incomplete" Cardiolipin Antigen (Cardchol).** [In English]

H. SCHMIDT and A. BIRCH-ANDERSEN. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **39**, 47–56, 1956. 22 refs.

In order to ascertain in which protein fraction of the blood syphilitic reagins occur, and to investigate the cause of the differences in the reactivity of sera to complete and incomplete cardiolipin antigens, electrophoretic fractionation of 10 sera which were thought to have given non-specific reactions with serological tests for syphilis and of 2 sera from patients with early syphilis was carried out at the State Serum Institute, Copenhagen. Quantitative tests were then carried out on the individual fractions by the Mørch–Wassermann technique with both cardiolipin antigen and "cardchol", an incomplete antigen composed of cardiolipin and cholesterol only. Previous work had shown that most syphilitic sera were more reactive with cardiolipin antigen, but that sera giving non-specific reactions often gave higher tires with cardchol than with the complete cardiolipin antigen.

Serological reactivity was demonstrated in both γ- and β-globulin components. It was found that some sera failed to react with cardiolipin before fractionation, although the γ- and β-globulin components were reactive. It is suggested that a factor was present in the albumin+α_1-globulin fraction which inhibited the reaction with cardiolipin but did not affect that with the incomplete antigen, thus offering an explanation of the lower specificity of cardchol. The greater sensitivity of cardiolipin with syphilitic sera may be due to the presence of more than one antilipoidal antibody.

It was not possible to show any correlation between the protein content of the fractions and their serological reactivity or to determine an electrophoretic pattern which indicated a positive reaction with lipoidal antigen.

A. E. Wilkinson

64. **Cardiolipin Antigen. Nephelometric Measurements. 4.** [In English]

A. REYN, J. HARTMANN, and H. SCHMIDT. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **39**, 57–66, 1956. 4 figs., 12 refs.

When saline suspensions of cardiolipin antigen are allowed to stand they become more sensitive and their turbidity increases owing to aggregation of particles, the progress of which can be followed by nephelometric measurements. This paper from the State Serum Institute, Copenhagen, describes experiments to determine the effect of serum and serum fractions on this process of maturation.

One part of cardiolipin antigen was mixed with 133 parts of saline, the serum fraction studied added immediately, and serial nephelometric measurements made over a 30-minute period. Human or guinea-pig serum at a concentration of 1 in 500 impaired maturation, syphilitic sera giving weaker reactions with the serum-treated antigen than with untreated antigen at the same interval after preparation. Tests on fractions separated from normal human sera by electrophoresis showed that the inhibitory effect of the albumin+α_1-globulin fraction on maturation was the strongest, being greater than that of the parent serum. The γ-globulin and $\gamma+\beta$-globulin fractions had no inhibitory effect.

Bovine albumin had no definite inhibitory effect on maturation, but syphilitic sera gave weaker reactions with antigen treated with it than with the control after 20 minutes' maturation. Bovine γ globulin inhibited maturation only in the highest concentration tested (1 in 50). Cohn's Fraction IV-1, containing 78% α globulins, produced complete inhibition of maturation at a concentration of 1 in 500; cardiolipin antigen treated with this serum fraction gave much less sensitive reactions with syphilitic sera than did untreated antigen. The authors consider that inhibition of nephelometric maturation and of serological activity may be connected with the presence of lipoproteins and that the effect is mainly located in the α globulins, more especially in the α_1 fraction.

A. E. Wilkinson

65. **Experiments on the Use of Hyperthermia in the Treatment of Primary and Secondary Syphilis.** (Опыт применения пиротерапии при первичном и вторичном сифилисе)

I. I. KHOKHUTKIN. *Вестник Венерологии и Дерматологии* [*Vestn. Vener. Derm.*] 32–33, No. 3, May–June, 1956.

Hyperthermia was employed in the treatment of early primary and secondary syphilis, in combination with penicillin in 44 cases and with arsenic and bismuth in 67 cases, at the Tomsk Medical Institute. The patients had had no previous antisyphilitic treatment. To induce fever TAB vaccine was injected intravenously, a course of 5 or 6 hyperthermic reactions, each lasting 5 to 10 hours and repeated every 3 to 5 days, being given. Penicillin was given intramuscularly in a dose of 40,000 units 3 hourly to a total of 5,000,000 units. As a rule, the combined treatment accelerated the disappearance of *Treponema pallidum* from eroded lesions and speeded up the regression of primary and secondary syphilides and enlarged lymph nodes. The serological reactions also became negative more rapidly. The results were better when hyperthermia was combined with penicillin than when metallotherapy was used, 2 patients failing to respond to the former and 5 to the latter. The maximum follow-up period was 7 years, though the number of patients kept under observation was never large and diminished steadily, only 6 patients in the first group and 3 in the second being followed up for longer than 5 years. Two patients in the first group and 10 patients in the second suffered a serological and clinical relapse within 6 months of treatment, and one patient in the second group developed asymptomatic neurosyphilis 16 months after completing treatment. The incidence of therapeutic failure was 9% in the first group and 23·8% in the second.

H. Makowska

Tropical Medicine

66. **Liver Function in Kwashiorkor**
A. A. KINNEAR and P. J. PRETORIUS. *British Medical Journal* [*Brit. med. J.*] **1**, 1528–1530, June 30, 1956. 38 refs.

Liver function tests were carried out in 107 cases of kwashiorkor at the Pretoria Hospital, South Africa. The serum total protein level was depressed to about 4 g. per 100 ml. and the albumin fraction to between 1·5 and 2 g. per 100 ml.—results strikingly similar to those obtained by others. The results of the thymol turbidity and thymol flocculation tests were of no diagnostic or prognostic significance. In 21% of the clinically cured cases the response to the thymol turbidity test changed from negative to positive at initiation of clinical cure and in 11% it remained positive throughout the illness. In many cases there was a marked but temporary rise in the thymol turbidity values between the 3rd and 15th days after treatment. The total serum lipid level rose in all cases during this period.

The results of the serum colloidal red and serum colloidal gold tests were essentially normal, and the van den Bergh reaction and serum bilirubin level were always within normal limits. The results of the " bromsulphalein " retention test—45 minutes being the interval allowed for complete disappearance of the dye—were of marked prognostic significance. In patients who recovered, bromsulphalein retention was usually normal within three days after treatment started. In the 19 fatal cases bromsulphalein retention was still abnormal at one week. *A. G. Shaper*

67. **Antibiotic Dietary Supplements in the Therapy of Childhood Protein Malnutrition**
R. A. LEWIS, M. P. BHAGAT, M. M. WAGLE, B. S. KULKARNI, and R. S. SATOSKAR. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 483–496, May, 1956. 3 figs., 21 refs.

Despite the beneficial effects of dietary supplements of animal protein in the treatment of kwashiorkor a moderate degree of anaemia which is unresponsive to conventional therapy often persists, the increased serum gamma-globulin concentration usually present may in some cases rise to an even higher level during treatment, and return of the serum albumin level to normal may be incomplete and delayed. In apparently healthy Indian students in Bombay there was an abnormal elevation of serum total and gamma-globulin values which could be correlated with a diet rich in vegetable protein. A daily dose of 50 mg. of one of the broad-spectrum antibiotics produced a fall in the serum globulin and a rise in the serum albumin levels in these students. The authors have therefore investigated the extent to which the administration of antibiotics may modify the course of protein malnutrition.

Two groups each of 10 children suffering from protein malnutrition, but not necessarily from typical kwashiorkor, were given a diet supplying 1,400 Cal. and containing 54 g. of protein daily, one group (Group A) receiving in addition 25 mg. of aureomycin or oxytetracycline daily. Patients in both groups were given vitamin A, nicotinic acid, penicillin, or blood transfusions where indicated, and several received injections of liver extract and vitamin B, and oral or intravenous iron. Those in the control group had the more vigorous anti-anaemic treatment and the larger amounts of penicillin.

In most of the patients in Group A there was a more rapid and extensive rise in the haemoglobin level, by an average of 3 g. per 100 ml. compared with 0·4 g. per 100 ml. in the control group. There was also an increase in the serum albumin level, the final mean value being 1 g. per 100 ml. higher than in the control group, while in most of those with an initially raised serum globulin level this value was lowered. In the control group serum albumin levels of 2·5 to 3·5 g. per 100 ml. remained fairly constant, but there was a tendency for the globulin level to rise during treatment. In general, the clinical response seemed more favourable in Group A and recurrence of diarrhoea was rare. There were 3 deaths in the control group, all of patients with very low levels of serum albumin, whereas none with equally low levels in Group A died.

The authors suggest that the change which takes place in the bacterial flora of the gastro-intestinal tract of infants at the time of weaning may precipitate protein malnutrition, and they recommend that the effects of antibiotic supplementation of diets low in animal protein be studied on a larger scale. *A. G. Shaper*

68. **RO 2-1160, a New Drug for the Treatment of Amebiasis**
D. T. MINTZ, J. W. MILLER, P. OTTOLENGHI, J. SCHACK, F. VAN ASSENDELFT, and H. MOST. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 497–500, May, 1956. 2 refs.

A new pentavalent aromatic stibonic acid (2-carboxymethylmercaptobenzene stibonic acid; RO 2-1160) has been tried clinically at the Tropical Disease Diagnostic Clinic, New York City Health Department, in the treatment of 195 patients (96% of them Puerto Ricans) with asymptomatic to moderately severe (16 cases) amoebiasis. After oral therapy, an average of 3 stools per case were examined, 20 patients being followed for less than 31 days, but the remainder were examined at intervals of one to 3 months for up to 12 months. One group of 159 patients received 25 mg. of the drug per kg. body weight for 5 successive days, with negligible toxic symptoms and a conversion rate of 73%. The remaining 36 patients received the same dosage for 10 days and showed a conversion rate of 94%. Toxic symptoms occurred in 6 patients in the latter group, however, and treatment

had to be discontinued in 4 of them because of nausea, vomiting, and diarrhoea. The drug did not appear to affect concurrent helminthic infestations. The authors suggest that a treatment schedule of 7 to 8 days " may be clinically acceptable ". *A. G. Shaper*

69. **The Use of Glaucarubin (a Crystalline Glycoside Isolated from *Simarouba glauca*) in the Treatment of Human Colonic Amebiasis**

F. VAN ASSENDELFT, J. W. MILLER, D. T. MINTZ, J. A. SCHACK, P. OTTOLENGHI, and H. MOST. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 501–503, May, 1956. 4 refs.

" Glaucarubin ", a crystalline glycoside which has been found to have amoebicidal properties *in vitro* and in experimental amoebiasis in animals, has been used at the Tropical Disease Diagnostic Clinic, New York City Health Department, in the treatment of patients with intestinal amoebiasis. Therapeutic evaluation was based on results in 85 cases considered to have been adequately followed up after treatment, though observations as to tolerance and toxicity were made on a total of 113 individuals treated. Initially 26 patients were given the drug orally in a dosage of 1 to 5 mg. per kg. body weight daily for 5 days, but as follow-up examination revealed a 58% failure rate this schedule was abandoned. A further 59 patients were treated for 10 days, 18 receiving a dosage of less than 5 mg. per kg. daily and 41 more than this amount, up to a maximum daily dose of 300 mg. An average of 2·6 stools per patient were examined during a mean follow-up period of 82 days. Cure rates of 62% and 73% were observed in the lower and higher dosage groups respectively. The drug had no effect on concurrent helminthic infestations. On the whole glaucarubin was well tolerated; in only 2 cases did vomiting necessitate the discontinuance of treatment, and one patient receiving 300 mg. per day developed transitory leucopenia. *A. G. Shaper*

70. **Clinical Trial of Diphenyl Thiourea Compound SU 1906 (Ciba 15095E) in the Treatment of Leprosy. Progress during the First Year**

T. F. DAVEY and G. CURRIE. *Leprosy Review* [*Leprosy Rev.*] **27**, 94–111, July, 1956. 5 figs., 4 refs.

The results are reported of a clinical trial carried out at Uzuakoli, Nigeria, of 4-butoxy-4′-dimethylaminodiphenylthiourea (SU 1906; thiocarbanilide) in the treatment of leprosy. This substance is almost tasteless, is sparingly soluble in water but highly soluble in acetone, and is given by mouth. Most of the patients had early or moderately severe lepromatous leprosy or spreading tuberculoid lesions. A skin biopsy was taken at the start of treatment and each patient was matched against a similar control patient treated with dapsone. SU 1906 was given initially in a daily dose of 1 g., which was increased by 0·5 g. at fortnightly intervals up to 3 g. daily on 6 days a week. Altogether the drug has been given to 41 patients for periods of 4 to 16 months, and has been well tolerated, the only toxic effect noted being a mild papular skin eruption which never lasted long.

Of 31 patients who had had no previous treatment, 21 were treated for more than 12 months and 27 for more than 6 months. Of the 17 patients with lepromatous lesions, all showed clinical improvement, which in 12 cases (70%) could be detected within 3 months, and in all cases was noticeable in the first 9 months, after which clinical and bacteriological improvement was slower. Marked improvement also occurred in the 8 tuberculoid cases, the improvement beginning in 1 to 4 months, and in 6 indeterminate and borderline cases. The complications during treatment included one case of erythema nodosum leprosum of short duration, and 3 cases of temporary increased activity of lesions at the 3rd month and in one case at the 7th month, while 12 patients complained of neuritis, usually between the 7th and 10th months, which disappeared spontaneously or on reduction of the dosage. A comparison showed that in 12 patients treated with SU 1906 for more than 12 months progress was as good as or slightly better than that in 12 controls treated with dapsone. The bacteriological progress of the patients is described in detail [for which the original must be consulted]; briefly, in the patients treated with SU 1906 it was equal to or slightly better than that of controls given dapsone.

It is considered that this compound deserves further careful study, since it appears to have the advantages of lack of toxicity and early activity, so that it would be suitable for initiating treatment. *F. Hawking*

71. **Observations on Forms of Parasitic Pharyngitis Known as " Halzoun " in the Middle East**

J. M. WATSON and R. A. KERIM. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **59**, 147–154, July, 1956. 3 refs.

Attention is drawn to the confusion which exists at present concerning the aetiology of a form of laryngopharyngitis peculiar to the Levant states, where it is known as " halzoun " (the Arabic word for a snail). The disease was first described in 1905 by the Lebanese physician Khoury, who suggested that the cause was a local infestation with *Fasciola hepatica*. The present authors have investigated the occurrence of the disease throughout the Republic of Lebanon and have studied the case histories of 23 individuals who had suffered attacks of halzoun relatively recently, although no case was actually observed by them. Two of the cases were due to infestation of the pharynx by the leech, *Linnatis nilotica*, and were cured by removal of the parasites. The remaining 21 cases followed the eating of raw sheep's or goat's liver and were considered to be due to pharyngeal infestation with very young specimens of *Fasciola hepatica*. The dominating symptom was pharyngeal discomfort, a " gripping " sensation unrelieved by coughing and ranging in intensity from tenseness and burning to considerable pain. Dysphagia, hoarseness, and aural symptoms were common, while dyspnoea, oedema of the face and neck, excessive lacrimation, and coryza were less frequent. The symptoms disappeared spontaneously in one to 7 days.

[This paper should be read in the original by those interested in this disease.] *C. L. Pasricha*

Allergy

72. **Anaphylactic Reactions in the Mesenteric Vessels of Guinea-pigs *in vivo*.** (Réactions anaphylactiques " in vivo " des vaisseaux mésentériques du cobaye)
J. LECOMTE. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **10**, 15–18, 1956. 3 refs.

The blood vessels of the mesentery of the guinea-pig can be used to observe the direct effect of an antigen–antibody reaction. In studies carried out at the University of Liège on guinea-pigs previously sensitized by injection of egg albumen it was found that the immediate vascular effects were similar to those observed in the rabbit—namely, accumulation of thrombocytes in the veins, with secondary embolism and rupture of the wall.

The administration of antihistamines did not modify the reaction. *A. W. Frankland*

73. **Acute Allergic Reactions Induced in Subjects with Hay Fever and Asthma by the Intravenous Administration of Allergens, with Observations on Blood Clot Lysis**
F. C. LOWELL, W. FRANKLIN, I. W. SCHILLER, and E. M. FOLLENSBY. *Journal of Allergy* [*J. Allergy*] **27**, 369–376, July, 1956. 2 refs.

In the treatment of 6 patients with allergic rhinitis or bronchial asthma at Evans Memorial Hospital (Boston University School of Medicine), Boston, intravenous injections of each patient's specific allergen were given in an initial dose of 0·005 Noon unit, which was then increased three- to ten-fold at each further injection until a reaction occurred. In all the patients an allergic reaction was obtained varying from mild, such as sneezing and obstruction of the nose, to severe, with coughing, wheezing, abdominal pain, urticaria, syncope, and frequency of defaecation and urination. There were no significant changes in the leucocyte count, the antibody titre, the complement titre, or the blood clotting time. In 3 cases fibrinolysis occurred, no visible clot being seen in drawn blood at the end of 24 hours. In 4 cases there were no significant changes in the pulse rate or blood pressure, and flushing of the skin was not marked in any of the cases. The skin sensitivity to the specific allergen was not changed by the injections.
H. Herxheimer

74. **Meticorten (Prednisone) and Meticortelone (Prednisolone) in the Treatment of Allergic Disorders**
C. E. ARBESMAN and R. J. EHRENREICH. *Journal of Allergy* [*J. Allergy*] **27**, 297–304, July, 1956. 12 refs.

At the General and Children's Hospitals, Buffalo, New York, prednisone and prednisolone were tried in the treatment of 101 patients, of whom 78 were suffering from asthma and the remainder from allergic rhinitis or allergic skin conditions. The doses employed were about one-third to one-fifth of those of cortisone and hydrocortisone. No difference in the effects of the two steroids was observed, and the maintenance dosage was, for the asthmatic patients, between 7·5 and 10 mg. per day. In the majority of cases the therapeutic results were " good " or " fair ". There was no nitrogen retention or potassium depletion, but prednisone in 9 cases and prednisolone in 10 cases caused gastro-intestinal symptoms, such as epigastric pain, nausea, or diarrhoea, which in 4 cases were severe enough to necessitate withdrawal of the treatment. *H. Herxheimer*

75. **Chlorpromazine in Asthma, Chronic Bronchitis and Emphysema**
J. A. CROCKET. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 221–224, July, 1956. 2 refs.

Chlorpromazine has been used by the author at the Glasgow Northern Hospitals in the treatment of 54 patients with bronchospasm since the end of 1954. Asthma was the main condition causing spasm in 39 cases, chronic bronchitis in 10, and pulmonary emphysema in 5. The patients included 3 who were under 21 and 31 who were over 40 years old, the average age of the 21 men being higher than that of the 33 women. All were treated as out-patients. The relative significance of emotional and allergic factors was assessed in each case [details of the method are not given]; in 38 cases emotional factors were deemed the more important and in 9 hypersensitivity, while in 7 cases both factors were regarded as " highly significant ". The initial dosage of chlorpromazine was 75 mg. daily [presumably by mouth], which was often increased to 100 mg. daily and occasionally to 200 mg. daily. Improvement, when it occurred, was observed within a few days of starting treatment and reached a maximum in 3 or 4 weeks; if no improvement had occurred by that time treatment was stopped; otherwise it was continued for an average period of 4 to 6 months. When necessary, treatment with bronchodilators or antibiotics or by desensitization was given concurrently.

Symptomatic improvement occurred in 24 of the 38 patients in whom the emotional factor predominated and in 4 of the 9 hypersensitive patients, while others improved in mental outlook and attitude without relief of respiratory symptoms and signs. Improvement was evenly distributed over all age groups and both sexes. Toxic reactions were slight and restricted to unpleasant sensations and dreams.

No evidence was obtained from this study to indicate that chlorpromazine has any direct influence on bronchitis or pulmonary emphysema with bronchospasm or on asthma due to hypersensitivity, although the author claims that it " often accentuated the effect of antihistamines ". When it was of value its action appears to have been due to the fostering of a more pacific mental status. *Raymond Parkes*

Nutrition and Metabolism

76. **Calorie Intake in Relation to Body-weight Changes in the Obese**

A. KEKWICK and G. L. S. PAWAN. *Lancet* [*Lancet*] **2**, 155–161, July 28, 1956. 13 figs., 14 refs.

The authors set out to determine which factor in reducing diets had the greater effect—restriction of calories or alteration in the proportions of protein, fat, and carbohydrate. The patients were manifestly obese, body weights being more than 35% above the standard for height according to the tables compiled by the Metropolitan Life Insurance Company. All were admitted to the Middlesex Hospital, London, but were allowed a moderate amount of exercise in the ward. After a period of stabilization the patients were divided into 3 dietetic groups. In Group 1 (6 patients) the proportions of protein, fat, and carbohydrate were kept constant and the total intake of calories was reduced; protein supplied about 20%, fat 33%, and carbohydrate 47% of the calories. The patients were kept on 2,000, 1,500, 1,000, or 500 Calories daily for periods of 7 to 9 days. In Group 2 (14 patients) there was a constant intake of 1,000 Calories a day, 90% being provided in turn by carbohydrate, fat, or protein. In both these groups water and sodium chloride were added to bring the total daily intake to 3,000 ml. and 10 g. respectively. In Group 3 (5 patients) a 2,000-Calorie diet was provided at first (to show that weight could be maintained at this level), and then the patients were given a high-fat, high-protein diet providing 2,600 Calories a day. The patients were weighed daily, and in some instances water, nitrogen, fat, sodium, chloride, and potassium balances were studied. The authors state that the results they report are selected, since a number of known failures in discipline were discarded.

The patients in Group 1 lost weight but remained in nitrogen balance. It was noted that during the period of weight loss the total available body water bore a constant relationship to body weight. Since carbohydrate could not account for the loss in weight, it was assumed that 33 to 50% of the weight loss in these patients was loss of available body water and the remaining 50 to 67% probably of fat. Patients in Group 2 lost weight rapidly when 90% of the calories were taken as protein or fat, but when carbohydrate provided 90% of the calories, weight was maintained. In Group 3 the patients were put on a 2,000-Calorie diet containing normal proportions of protein, fat, and carbohydrate. Over a period of 7 days they either maintained their weight or gained a little. The intake was then increased to 2,600 Calories daily, but the proportions of the diet were altered by increasing the amounts of protein and fat and reducing the amount of carbohydrate. In spite of the increase in calories 4 of the 5 patients lost weight, 30 to 50% of this being shed as available body water. The rate of insensible loss of water was found to rise with a high-fat, high-protein diet and to fall with a high-carbohydrate diet. There were no defects in absorption to account for the weight loss, and the authors suggest that the metabolism of the obese alters with the composition of the diet. *Norval Taylor*

77. **Carbon Balance. A Clinical Approach to Energy Exchange**

J. M. KINNEY and F. D. MOORE. *Surgery* [*Surgery*] **40**, 16–26, July, 1956. 8 figs., 7 refs.

A method of calculating carbon balance which provides direct evidence of energy utilization in the surgical patient is described in this paper from Harvard Medical School and Peter Bent Brigham Hospital, Boston. A closed-circuit apparatus was used for measuring the patient's output of carbon dioxide, which was absorbed by means of an alkali spray. Clinically, carbon dioxide output was determined during a number of 7-minute periods throughout three separate days, first with the patient taking his normal diet, then with the patient fasting, and again while he received his normal diet through a feeding tube at varying rates. The total amount of carbon dioxide expired daily was estimated by applying a planimeter to the area under the curve constructed from the individual estimations. A positive carbon balance was noted on both feeding days, the carbon output being reduced by fasting. *C. L. Cope*

78. **Fat Absorption in Chronic Severe Malnutrition in Children**

F. GÓMEZ, R. RAMOS GALVÁN, J. CRAVIOTO, S. FRENK, J. VÁZQUEZ SANTAELLA, and C. DE LA PEÑA. *Lancet* [*Lancet*] **2**, 121–122, July 21, 1956. 2 figs., 13 refs.

The fat balance of 14 children [age not specified] suffering from severe chronic malnutrition was studied at the Hospital Infantil, Mexico City, over periods of 4 days on admission and during convalescence; in 10 cases an additional study was carried out after a week's hospital treatment. Although macroscopic steatorrhoea was present in only a few cases on admission, all the patients had chemical steatorrhoea, fat absorption varying from 25 to 75% of the intake. The steatorrhoea improved with dietary treatment, 72 to 88% of the dietary fat being absorbed after about 6 weeks. Moreover, the absolute amount of fat absorbed was greatly increased, as the fat intake after recovery was much greater than on admission. At all times there was a strong positive correlation between the intake of fat (ranging from 20 to 150 g.) and the proportion absorbed. The authors therefore suggest that the reduction of fat intake in the steatorrhoea of malnourishment is unnecessary and possibly undesirable. *M. Lubran*

79. **Endocrine Disturbances in Malnutrition**

S. ZUBIRÁN. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **46**, 1021–1024, Aug., 1956. 17 refs.

Gastroenterology

80. The Etiology and Histogenesis of Carcinoma of the Esophagus

P. E. STEINER. *Cancer* [*Cancer (Philad.)*] **9**, 436–452, May–June, 1956. 21 figs., 45 refs.

A study of possible aetiological factors was made in 116 cases of cancer of the oesophagus occurring among 9,000 consecutive necropsies performed at the University of Chicago.

From a comparison of the findings in these 116 cases with those in matched control groups containing the same number of cases of cancer of the stomach, cancer of the lung, malignant lymphatic disease, and non-cancerous disorders respectively there appeared to be statistically significant associations between oesophageal cancer and (1) a second primary cancer of the upper alimentary tract; (2) polyps of the large intestine (perhaps an indication of an inherently high susceptibility of the alimentary tract to neoplastic transformation); (3) cirrhosis of the liver; and (4) a history of alcoholism. A history of heavy tobacco smoking was found as frequently in this group as in the group with cancer of the lung, but only half as frequently in the other three groups.

In conformity with similar series which have been reported in the literature it was found that males were affected twice as frequently as females, and that no racial, geographical, occupational, or other factors appeared to be of significance.

A histological study was made of 8 clinically silent small oesophageal cancers occurring in this series, together with one additional case, to determine the earliest phases of the growth. The tumours seemed to be associated for the most part with atrophic mucosa and with subepithelial fibrosis. Their manner of origin resembled that of cancer arising in a scar more closely than that of carcinoma *in situ*. Although it is concluded that carcinoma of the oesophagus is of multifactorial origin, the importance of non-specific trauma acting over a long period is emphasized.

J. B. Cavanagh

81. Effect of Cigarette Smoking on Gastric Secretions of Patients with Duodenal Ulcer

P. COOPER and J. B. KNIGHT. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 17–21, July 5, 1956. 9 refs.

The effects of cigarette smoking on the volume, *p*H, free acid, peptic concentration (units per ml.), and peptic output (units per 30 minutes) of gastric secretion was studied in 147 male patients with proven duodenal ulcer at the Veterans Administration Hospital, Providence, Rhode Island.

In the first part of the investigation 60 patients smoked normally for 30 minutes, an average of 2½ cigarettes being smoked, and 60 patients (including 16 non-smokers) refrained from smoking during this period. All had fasted overnight. For both groups there was a preliminary 30-minute basal period, and the test half-hour was followed by two 30-minute periods without smoking. There were no statistically significant differences between the groups in any of the values recorded. This, in the authors' view, was the most important finding.

In the second part of the investigation changes in the *p*H of gastric juice after smoking and after broth and insulin stimulation were studied in 16 patients before and 11 patients after partial gastrectomy for duodenal ulceration. Both broth and insulin stimulation caused a reduction in *p*H in the preoperative group; in the postoperative group a slight reduction in *p*H followed broth stimulation and a further reduction followed insulin stimulation. During a 30-minute smoking period there was a rise in the *p*H of gastric secretion in both groups.

J. Warwick Buckler

82. Studies in Ammonia Metabolism. I. Ammonia Metabolism and Glutamate Therapy in Hepatic Coma

B. EISEMAN, W. BAKEWELL, and G. CLARK. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 890–895, June, 1956. 2 figs., 31 refs.

The authors, from the University of Colorado Medical School and the Veterans Administration Hospital, Denver, report a study of the blood ammonia concentration in 31 cirrhotic patients in 44 episodes of hepatic coma, in 15 with advanced cirrhosis not in coma, and in 25 controls without hepatic disease. The control blood ammonia level lay between 0·9 and 2 μg. per ml., and in 12 of the 15 cirrhotics without coma the values were within these limits. In 40 out of 44 episodes of coma the blood ammonia level was raised. No increase was noted in the level in 3 patients in typical hepatic coma, although 2 died in coma. Ingestion of ammonium citrate had no effect in controls, but resulted in an increase in the blood ammonia concentration to an average of 3·6 μg. per ml. in cirrhotics, with production of flapping coma in one; there was a return to normal within 6 hours.

In general, the clinical course of hepatic coma was reflected in a raised blood ammonia concentration; in a number of cases, however, this was not so, and normal values were recorded. Of 31 patients in coma given sodium glutamate, only 9 benefited. It is suggested that at least two types of hepatic coma may occur. The first is precipitated by administration of exogenous ammonium salt or protein; it is associated with high blood ammonia concentrations and responds promptly to glutamate therapy, being due to ammonia intoxication. The second occurs during spontaneous hepatic failure, is not necessarily associated with a high blood ammonia level, and seldom responds to glutamate therapy.

W. H. Horner Andrews

83. **Relationship of Portal Hypertension to Ascites in Laennec's Cirrhosis**
W. J. EISENMENGER and W. F. NICKEL. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 879–889, June, 1956. 5 figs., 7 refs.

The effect of porta-caval anastomosis on the fluid and electrolyte balance was studied at the Rockefeller Institute for Medical Research and the New York Hospital in 5 patients with Laënnec's cirrhosis and chronic ascites. Some of the patients had undergone paracentesis on a number of occasions, and 3 suffered from bleeding oesophageal varices. Sodium retention was demonstrated in all 5, and some degree of control of the ascites was possible by restricting sodium intake. After operation the ascites disappeared in each case, and in 3, at any rate, sodium excretion increased markedly. Peripheral oedema was present throughout in one case and developed after operation in 3, being possibly related to hypoalbuminaemia in 2.

In 2 additional cases, apparently characterized by an abnormally increased hepatic lymph flow, porta-caval anastomosis resulted in ascites. In one of these there was hepatic venous endophlebitis; in the other, ascites was transient and possibly due to damage to lymph vessels.

The authors consider that in patients with chronic ascites due to Laënnec's cirrhosis the various mechanisms responsible for abnormal retention of sodium and water by the kidney are secondary to, rather than the cause of, ascites. *W. H. Horner Andrews*

84. **Pancreatic Steatorrhoea. Pancreatic Diabetes and the Effects of Pancreatic Steatorrhoea on the Organism.** (Les stéatorrhées pancréatiques. Le diabète pancréatique et les répercussions des stéatorrhées pancréatiques sur l'organisme)
P. A. BAUER. *Annales de médecine* [*Ann. Méd.*] **57**, 113–146, March–April, 1956. Bibliography.

The author presents, from the University Medical Polyclinic, Geneva, a report on 14 cases of pancreatic steatorrhoea, with a brief discussion of the prognosis and treatment of this disease. Pancreatic diabetes with glycosuria was present in 6 of the 14 cases, and a hyperglycaemic curve was obtained in only 2. Insulin requirements were low, and no retinal or renal changes were found. Changes in the blood lipid concentration were observed in 5 out of 10 cases in which the serum cholesterol level was estimated, the value being below normal in 4 cases and above normal in one. Blood counts, carried out on 13 patients, were considered normal in only 2 cases, 7 showing normochromic anaemia, 3 hypochromic anaemia, and one macrocytic anaemia. Determination of the serum protein content in 11 cases showed that there was hypoproteinaemia in 3, the albumin level being low in 2 and the globulin level high in one. Osteomalacia was found in 5 out of 10 cases examined by biopsy, osteoporosis in one, and what is termed "simple senile osteoporosis" in 2, in both of which it was associated with carcinoma; in only 2 cases were the bones considered to be normal. Two patients were suffering from tetany. Disturbances of the peripheral nervous system were present in 5 cases, with onset in one case 4 years before steatorrhoea was observed, though diabetes was present. In the other 4 cases the lesions were detected at the same time as the steatorrhoea, and were associated with markedly poor general nutrition, 2 of the patients being diabetic and one an alcoholic. Liver damage was absent in only 3 of the 14 cases. Cirrhosis [assuming that "atrophy" implies cirrhosis] was present in 6 cases, tuberculosis in 2, and "chronic stasis" in one. Gall-stones were found in 3 cases.

Steatorrhoea is regarded as a late complication of chronic pancreatitis, the average age of the patients being 59 and the age range 44 to 79 years. The expectation of life after its appearance is from one to 5 years, with an average of 2 years; 2 of the author's patients have survived 4 and 5 years respectively. Malnutrition resulting from the syndrome was considered to have led to active tuberculosis in 3 cases. The treatment recommended is a high-calorie diet with low fat content, together with the administration of pancreatic extract, emulsifying agents, insulin when diabetes is present, liver extract, calcium, vitamins, and lipotropic agents, for example, methionine, and in some cases steroid therapy.

[Much of this paper consists of a review of other workers' findings and theories. For example, the sections devoted to radiological findings and calcium and phosphorus metabolism merely review the relevant literature, and no significant figures for the results of biochemical investigations are reported.]
W. A. Bourne

85. **The Ulcerogenic Tumor of the Pancreas**
E. H. ELLISON. *Surgery* [*Surgery*] **40**, 147–169, July, 1956. 4 figs., 21 refs.

A syndrome characterized by fulminating and recurrent peptic ulceration associated with a non-insulin-producing islet-cell tumour of the pancreas is described. The literature contains reports of 19 cases of this syndrome, and a recent review of all clinical and necropsy records over the last 10 years at the Ohio State University Medical Center, Columbus, Ohio, revealed 5 further cases, all 24 being discussed in the present paper. The gastric acidity in these cases was very high and the site of ulceration often atypical—in several instances the site of the primary ulcer was the jejunum. Neither medical nor surgical treatment prevented recurrent ulceration in 9 patients, who underwent a total of 23 operations; all 9 patients died from ulceration and at necropsy a pancreatic tumour was found in each case. In 11 other cases a similar tumour was found and removed at operation; the tumour recurred in 3 of these. Of the 24 pancreatic tumours, 14 were single and 10 were multiple; they involved the entire pancreas, or the head and body, or the body and tail. One tumour arose in aberrant pancreatic tissue in the stomach. Although 19 of the 24 islet-cell adenomata were malignant, they were slow-growing, and peptic ulceration remained the predominant manifestation in nearly all the cases. *Guy Blackburn*

Cardiovascular System

86. **Anomalous Pulmonary Venous Drainage**
J. B. HICKIE, T. M. D. GIMLETTE, and A. P. C. BACON. *British Heart Journal* [*Brit. Heart J.*] **18**, 365–377, July, 1956. 7 figs., 50 refs.

In cases of anomalous pulmonary venous drainage, which in the great majority occurs only in the right lung, the veins generally enter the right atrium or superior vena cava; associated atrial septal defect is common. If the veins from the left lung are abnormal they generally enter the coronary sinus or a left-sided superior vena cava. The physiological effect is similar to that of an atrial septal defect, namely, a shunt of oxygenated blood into the right atrium, increased pulmonary blood flow, right ventricular hypertrophy, and commonly incomplete right bundle-branch block. Pulmonary hypertension may occur, and if an atrial septal defect is present the shunt through this may reverse, causing cyanosis.

In this report from St. Thomas's Hospital, London, 13 cases are described, in none of which was the anomalous venous drainage total; in 11 cases the anomaly was on the right and in 2 on the left, and confirmation at operation or necropsy was obtained in 9. Atrial septal defect was present in at least 9 cases. The patients, whose ages ranged from 10 to 50 years, all presented with exertional dyspnoea, 7 were cyanosed, and 3 had signs of right heart failure. The physical signs, electrocardiograms, and radiological findings were similar to those of atrial septal defect. In one case radiography revealed aneurysmal dilatation of the superior vena cava which disappeared when the abnormal blood flow into it was stopped. In the authors' experience the diagnosis can rarely be made on the clinical findings alone, and must depend upon special methods such as cardiac catheterization (the most informative), angiocardiography, or the study of dye dilution curves. Surgical treatment may be by ligation of a single anomalous vein or of the artery and veins to one lung, or by pneumonectomy; closure of the atrial septal defect may be necessary or attempts may be made to redirect the abnormal venous return. Of the 8 patients in this series whose subsequent course is mentioned, 5 have died and 3 have been improved by surgery. *J. A. Cosh*

87. **Cardiocirculatory Studies in Pulsus Alternans of the Systemic and Pulmonary Circulations**
M. I. FERRER, R. M. HARVEY, A. COURNAND, and D. W. RICHARDS. *Circulation* [*Circulation* (*N.Y.*)] **14**, 163–174, Aug., 1956. 14 figs., 10 refs.

Studies carried out in 21 patients have indicated that alternation of the pulse pressure in man can occur independently in either the greater or the lesser circulation without appearing in the other. Even when bilateral alternation exists, this cyclic variation may disappear in one circulation while persisting in the other. Although pulmonary or systemic hypertension was frequently associated with pulmonary and systemic alternans respectively, hypertension was not invariably present. Furthermore, changes in lesser or greater circulation pressures bore no consistent relationship to the appearance or disappearance of pulsus alternans. Mechanisms responsible for pulsus alternans, in particular variations in stroke volume and vascular pressures, were considered, but no single explanation satisfied the facts revealed in this study.—[Authors' summary.]

88. **Botkin's [Abrams's] Heart Reflex and Variability of Heart Size.** (О кожно-сердечном рефлексе Боткина и изменчивости размеров сердца)
G. M. POKALEV. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 36–40, No. 4, 1956. 1 fig., 2 refs.

Abrams's heart reflex was studied by standard and teleradiography in 22 control subjects and 163 patients suffering from hypertension, "rheumatism", peptic ulcer, and chronic gastritis at the Kirov Medical Institute, Gorky. The skin over the praecordium, left shoulder, and left scapula was irritated for 5 minutes with a rubber sponge or brush. The reflex changes in the size of the heart shadow varied from insignificant values of 0·4 to 0·6 cm. to 2·0 to 2·6 cm., "longitudinally and across". The reflex manifested itself not as a simple increase or reduction in the size of the cardiac shadow, but as a multiphasic, gradually fading response lasting 30 to 40 minutes.

In patients with acute rheumatism and hypertension the initial response was an increase, and during remissions a decrease, in the size of the heart shadow. The general condition of the vegetative nervous system is considered to determine the amplitude of the response.
A. Swan

89. **A Simple, Expendable Blood Oxygen–Gas Exchanger for Use in Open Cardiac Surgery**
I. W. BROWN, W. C. HEWITT, G. YOUNG, W. C. SEALY, and J. S. HARRIS. *Surgery* [*Surgery*] **40**, 100–111, July, 1956. 9 figs., 12 refs.

In developing the technique of extracorporeal circulation for the purposes of open heart surgery the authors have attempted to construct a blood–gas exchanger for use with a dual pump which should be: (1) free from dependence on mechanical or electronic devices; (2) simple and hand-operated; (3) not subject to bacterial or pyrogen contamination and capable of steam-autoclave sterilization; (4) provided with smooth, non-wetting surfaces throughout, to minimize damage to the blood elements; (5) capable of permitting flow rates of up to 1,500 ml. per minute; and (6) cheap and expendable. The exchanger finally developed at Duke University School of Medicine, Durham, North Carolina, consists of a polyvinyl plastic bag, 1,200 ml. in capacity, of a type recently introduced in the U.S.A. as a blood

container, the internal surface area being increased by the inclusion of a skein of sealed polythene tubing coated with " antifoam A ". Into this is fed 640 ml. of pure oxygen at atmospheric pressure, followed by 500 ml. of venous blood. Gentle rocking of the bag permits full oxygenation of the blood in 1½ minutes.

The operation is started with a reserve of, say, 4 such containers filled with heparinized, oxygenated blood which is fed by the first pump through a bubble trap and water bath into the patient's arterial circulation. At the same time vena caval blood from the patient passes through the second pump and is collected in exchanger bags containing oxygen which are weighed when full and hung up to be connected in series to the arterial return.

This system can be worked by two assistants, one changing the outflow bags and monitoring the outflow rate, the other being responsible for the inflow. A flow rate of 35 ml. per kg. body weight per minute can be maintained, with 99% oxygen saturation. Experimental studies on dogs and observations made on one patient during cardiac surgery have shown that the plasma fibrinogen level remains normal, and that the platelet count is reduced by only 50% as a result of use of the oxygenator. *C. A. Jackson*

90. A Clinical Study of the Action of Aminomethylheptanol in Certain Types of Cardiac Insufficiency. (Recherches cliniques sur l'action de l'amino-2-méthyl-6-heptanol-6 dans certaines insuffisances cardiaques)
—. LANGERON and —. ROUTIER. *Presse médicale* [*Presse méd.*] **64**, 1371–1372, Aug. 4, 1956. 6 figs., 8 refs.

It has been shown that " heptaminol " (amino-2-methyl-6-heptanol hydrochloride) directly increases the force of cardiac contraction, augments the coronary flow, exerts a direct tonic action on the peripheral vessels, and promotes diuresis. The action of the drug is short-lived and it is rapidly excreted. In the treatment of cardiac conditions 20 ml. of heptaminol dissolved in 250 ml. of glucose solution is slowly infused intravenously over a period of 3 or 4 hours, one infusion being given daily generally for 20 days, after which the drug may be administered by mouth or by intramuscular injection for a further 15 days.

From the University of Lille the authors report the use of this drug in the treatment of 13 cardiac patients, 9 of whom were suffering from chronic pulmonary heart disease. The results of treatment were assessed clinically, electrocardiographically, and by measurement of the venous pressure, the circulation time, and the urinary output. They were judged to be " excellent " in 4 cases and " very good " in 7 others, 8 of the 9 patients with cor pulmonale showing striking improvement. Successful treatment was accompanied by a reduction in the venous pressure and circulation time and by an increased output of urine. No toxic effects were observed. Retrosternal pain was ameliorated in one patient with left ventricular failure. The action of heptaminol in " global cardiac insufficiency " is said to resemble that of ouabain in its rapidity and duration of action. Heptaminol is particularly recommended for the treatment of right ventricular insufficiency, in which condition it is claimed to reduce pulmonary hypertension. *Bernard Isaacs*

CONGENITAL HEART DISEASE

91. The Valve of the Inferior Vena Cava
J. B. HICKIE. *British Heart Journal* [*Brit. Heart J.*] **18**, 320–326, July, 1956. 6 figs., 24 refs.

During the attempted repair of atrial septal defect at St. Thomas's Hospital, London, by the atrioseptopexy operation of Bailey in 2 men aged 47 and 27 years respectively, in both of whom there was, in addition, anomalous insertion of the right pulmonary veins into the right atrium or superior vena cava, the accurate identification of the inferior margin of the defect by the surgeon's finger was made difficult by the presence of a well-developed valve at the opening of the inferior vena cava (Eustachian valve). In neither case could a satisfactory repair be made and both patients died.

The Eustachian valve (first recognized by Bartolomeno Eustachius in 1563 and later accurately described by Winslow in 1717) runs obliquely across the floor of the right atrium, starting postero-laterally in front of the orifice of the inferior cava and rising crescentically to be inserted into the medial wall in front of the fossa ovalis. In one of the present cases it virtually divided the atrium into two, being 6·2 cm. long on its crescentic margin, 2·1 cm. wide, and 0·5 cm. thick at its base. In the other case the valve was muscular, 4·7 cm. long, 1·5 cm. wide, and 0·7 cm. thick, and on blind palpation was mistaken for the inferior margin of the septal defect. The importance of recognizing the presence of the valve in attempting repair of atrial septal defect is emphasized.

The embryological development of the Eustachian valve is described, and the various theories regarding its action and the effect of its persistence into adult life are discussed. *J. A. Cosh*

92. Bodily Development in Congenital Heart Disease. (Zur Frage der körperlichen Entwicklung bei angeborenen Herzfehlern)
A. SCHAEDE, H. LOTZKES, and H. H. HILGER. *Archiv für Kreislaufforschung* [*Arch. KreislForsch.*] **24**, 1–26, June, 1956. 18 figs., 28 refs.

In an investigation carried out at the University Medical Clinic, Bonn, 750 young patients with congenital heart disease were seen between 1948 and 1953, of whom 576 who had been examined by means of angiocardiography and cardiac catherization were further studied with regard to their subsequent bodily development as shown by body weight and height. They were classified into three groups: (1) those with no shunt (41 cases), (2) those with left-to-right shunt (117 cases), and (3) those with right-to-left shunt (418 cases), Group 3 being further subdivided according to (*a*) the severity of cyanosis and anaemia and (*b*) the pulmonary blood flow.

It was found that in all these patients bodily development was grossly reduced, weight being more affected

than height. The cause of underdevelopment was assumed to be the hypoxaemia resulting from the continuous cyanosis and this was confirmed by the results of estimations of the systemic circulatory minute volume. It was shown that the degree of developmental disturbance and shortening of the expectation of life were correlated with the degree of cyanosis. On the other hand the degree of diminution in the pulmonary blood flow bore no relation to the development of lung defects. The most severely affected patients were those with cyanotic heart disease associated with auricular defect. In these cases the girls were less underdeveloped than the boys and relatively twice as many girls reached adult life, an observation which leads the authors to conclude that hypoxaemia is less harmful to the female than to the male. *D. Goldman*

CHRONIC VALVULAR DISEASE

93. **Rheumatic Tricuspid Stenosis. A Clinical and Physiologic Study with a Suggested Method of Diagnosis**
A. REALE, H. GOLDBERG, W. LIKOFF, and C. DENTON. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 47–56, July, 1956. 5 figs., 19 refs.

From Hahnemann Medical College, Philadelphia, the authors report the results of clinical studies of 13 and of haemodynamic studies of 10 patients with rheumatic tricuspid stenosis, all confirmed at operation or necropsy. Exertional dyspnoea, fatigue, and peripheral oedema were the commonest symptoms, and cervical venous distension and hepatic enlargement the commonest signs. All patients with a diastolic murmur at the tricuspid area had concomitant mitral stenosis, and a few had radiological evidence of right atrial enlargement.

The arterio-venous oxygen difference was increased in 6 out of 9 cases; the resting cardiac index was low in 7 and was not raised by exercise in the 2 cases in which this was tested. The mean resting pulmonary arterial pressure was raised in 7 cases, and in one in which it was normal exercise raised it excessively. Pulmonary capillary wedge pressures were raised in 5 out of 7 patients, as was also pulmonary arteriolar resistance in 5. In 4 patients there was a raised right ventricular end-diastolic pressure. The resting mean right atrial pressure was markedly raised in 8 out of 10 patients, and in 2 of these exercise caused it to rise still higher. Two types of right atrial pressure pulse were observed: giant "a" waves with otherwise normal pattern in all cases of sinus rhythm, and a diphasic positive systolic rise (resembling a ventricular pressure pulse) in 3 patients with atrial fibrillation, only one of whom had tricuspid regurgitation. In 2 cases normal "x" waves accompanied a minor degree of regurgitation.

The diastolic pressure was higher in the right atrium than in the right ventricle in all of 9 patients, and in the one patient in whom the effect of exercise was studied this increased the atrio-ventricular gradient. The calculated area of the tricuspid valve (by the method of Gorlin) did not correlate well with that found at operation. A successful attempt was made in one patient to estimate the tricuspid area at cardiac catheterization by means of a rubber balloon filled with radio-opaque dye.

The authors conclude that tricuspid stenosis does not protect patients with mitral disease from the effects of altered pulmonary dynamics, except perhaps from actual pulmonary oedema. They suggest that the jaundice, oedema, ascites, and hepatomegaly in these cases are caused by right ventricular failure rather than by the tricuspid stenosis *per se*. *D. Emslie-Smith*

94. **Postcardiotomy Syndrome in Patients with Rheumatic Heart Disease. Cortisone as a Prophylactic and Therapeutic Agent**
D. T. DRESDALE, C. B. RIPSTEIN, S. V. GUZMAN, and M. A. GREENE. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 57–74, July, 1956. 33 refs.

The syndrome which occurs after cardiotomy in patients with rheumatic heart disease is discussed in this paper from Maimonides Hospital of Brooklyn and the State University of New York. It is characterized by fever and pleuropericardial chest pain, congestive heart failure, pleural effusion, polyarthritis, arrhythmia, abdominal pain, subcutaneous nodules, haemoptysis, and psychosis; there is laboratory evidence of a non-specific inflammatory process. In the majority of cases the initial episode is observed within one month of operation, and recurrences may appear up to 28 months afterwards.

A series of 84 patients (26 men) with mitral-valve disease who were subjected to cardiotomy were observed; 58 had pure mitral stenosis, and in 48 rheumatism was considered to be completely inactive. Of the 84 patients, 58 were given cortisone prophylactically in a dosage of 75 to 300 mg. daily for 3 to 6 weeks after operation, while 26 served as controls. The syndrome occurred in 8 of the controls; in the cortisone-treated group it occurred while the drug was being taken in 4 and after the drug was withdrawn in 17. Although the syndrome developed in 2 patients in whom there was clinical evidence of active rheumatism before operation, there was no clear correlation between the incidence of the syndrome and the preoperative evidence of possible rheumatic activity or the presence at operation of Aschoff bodies in the auricular appendage.

Once established, the course of the syndrome was unaffected by antibiotic therapy and was not definitely influenced by salicylates or amidopyrine (" pyramidon "), although these produced gradual and partial reduction in temperature. Cortisone (50 to 300 mg. daily) was given as a therapeutic measure to 21 patients during 65 attacks of the syndrome; in 62 of these attacks fever subsided in 24 to 36 hours. Adequate doses of the hormone brought about dramatic relief of pain in the chest and joints, but did not affect pleural or pericardial effusions or the chest pain and fever ordinarily associated with thoracotomy. Occasionally the addition of cortisone to a treatment regimen appeared to abolish arrhythmia or to lessen the degree of heart failure. Although 3 patients needed cortisone almost continuously for 5 to 12 months, no undesirable side-effects

were noted. There were 2 deaths in the control group, while in the treated group there was one death from pulmonary oedema 16 days after operation; in this last case florid rheumatic endocarditis and myocarditis were found post mortem, and the authors consider that the dosage of cortisone given was too low.

It is suggested that the syndrome results from trauma to a heart already affected by rheumatism, although, as the authors point out, it differs from rheumatic fever in several important respects. *D. Emslie-Smith*

95. **The Surgical Treatment of Mitral Insufficiency with Particular Reference to the Application of a Vertically Suspended Graft**

W. W. L. GLENN, T. O. GENTSCH, M. HUME, and P. H. GUILFOIL. *Surgery* [*Surgery*] **40**, 59–76, July, 1956. 12 figs., 8 refs.

The authors have previously reported experimental work in the treatment of mitral insufficiency by means of a tubular vascularized graft made from a functioning segment of internal mammary artery and vein inserted through the left ventricle and passing through the orifice of the mitral valve, its upper end being secured in the left atrium.

In the present paper from Yale University School of Medicine they report further experiments with this type of prosthesis, using a graft made of compressed "ivalon" sponge, uncovered or covered with pericardium or with inverted segments of autogenous vein. In dogs in which mitral insufficiency had been produced artificially the uncovered sponge was rapidly covered by ingrowths of fibroblasts, but the graft covered with inverted vein was more satisfactory, producing minimal damage to the valve cusps in the early postoperative period. Ultimately the graft became a solid, vascularized, transventricular column covered with endothelium.

It was calculated that a graft of this type 2 cm. in diameter placed with care in the regurgitant stream would give adequate control of mitral insufficiency in man without causing obstruction to the flow, and the experience gained from three such operations on gravely incapacitated patients is reported. Two patients survived, but the evidence of improvement was equivocal. The main difficulty has been in obtaining sections of vein sufficiently long to cover the graft. This experimental work is being continued. *C. A. Jackson*

96. **The Influence of Mitral Regurgitation on the Results of Mitral Valvotomy**

J. R. BELCHER. *Lancet* [*Lancet*] **2**, 7–11, July 7, 1956. 2 figs., 18 refs.

The results of mitral valvotomy in 52 patients with mitral incompetence were compared with those obtained in 100 patients operated on for pure stenosis. The state of the valve was fully assessed with the finger before operation. The degree of regurgitation was noted and the cases classified in 4 grades, while the degree of stenosis was recorded on a 5-point scale. On the basis of mobility the valves were classified as hypermobile, diaphragmatic, or immobile. After valvotomy the degree of split was assessed and the degree of regurgitation reassessed.

In cases in which a diaphragmatic valve was found the results of valvotomy were fairly good, even when incompetence was dominant; the degree of regurgitation was increased by the operation in relatively few instances. On the other hand the results in cases of hypermobile and immobile valves were poor, and the author suggests that if the presence of such valves can be confidently diagnosed surgery should not be undertaken. Traumatic mitral incompetence was caused by valvotomy in 10 cases, but this had little influence on immediate results, the dominant factor being the efficacy of the split. The severity of the postoperative incompetence had more influence on the late results.

There were 7 operative deaths and one late death among the 100 patients with pure stenosis and 3 operative and 6 late deaths among those with incompetence (most of the deaths in the latter group occurred in patients with hypermobile and immobile mitral valves).

The mechanism of production of the clinical signs and the differential diagnosis of the three types of valve are discussed. It is concluded that the clinical diagnosis of the anatomical type of valve may be possible, that valve mobility plays a dominant part in operability, and that commissurotomy is all that is necessary where a diaphragmatic valve is found; in cases in which diagnosis of one of the other types of valve can be made with certainty operation should be withheld until suitable methods of treatment have been developed.

F. J. Sambrook Gowar

97. **Mitral Valvotomy. A Progress Report**

R. W. D. TURNER and H. R. L. FRASER. *Lancet* [*Lancet*] **2**, 526–531 and 587–592, Sept. 15 and Sept. 22, 1956. 11 refs.

CORONARY DISEASE AND MYOCARDIAL INFARCTION

98. **Plasma Lipids and Proteins and Their Relationship to Coronary Disease among Navajo Indians**

I. H. PAGE, L. A. LEWIS, and J. GILBERT. *Circulation* [*Circulation (N.Y.)*] **13**, 675–679, May, 1956. 2 figs., 8 refs.

A review of the hospital records showed that myocardial infarction was diagnosed in only 5 full-blooded Navajo Indians among 10,267 admissions over 4 years to the Navajo Medical Center Hospital, Fort Defiance, Arizona, and even in these 5 cases it was not confirmed by electrocardiography. Again, not one case of coronary arterial disease was observed among 60,405 out-patient attendances. In contrast, out of 20,289 white patients admitted to St. Joseph's Hospital, Albuquerque, New Mexico (about 150 miles distant), 146 had myocardial infarction; the age distribution was similar in the two groups. The Navajos are well nourished, and usually eat a typically American diet, often containing foods of high cholesterol and high fat content; they tend to consume less fruit and vegetables but more fried food.

The mean plasma total protein level among the Navajos was only slightly lower than that among a group of persons from Cleveland, Ohio; the albumin level was lower (3·21 to 3·53 g. per 100 ml. compared with 4·74 g. in Cleveland), while the globulin level tended to be slightly higher, especially the α- and γ-globulin fractions. The lipoprotein components were also very similar in the two populations, except that the fractions Sf_{25-40} and Sf_{1-10} (corresponding to β_1 and α_1 lipoprotein) was somewhat lower in the Indians. The mean total cholesterol value was about 50 mg. per 100 ml. lower in the Navajo group than in the Cleveland group and did not alter with age in either group. It is concluded that the lower serum cholesterol levels and the extremely low incidence of coronary arterial disease among the Navajo Indians clearly cannot be attributed to a lower intake of fat, and the authors suggest that hereditary factors may be responsible.

Robert de Mowbray

99. **The Natural History of Changing Patterns of Angina Pectoris**
H. LEVY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 1123–1135, June, 1956. 19 refs.

A study was made of 158 patients with coronary arterial disease in whom an established pattern of anginal pain had recently undergone a sudden change or whose angina had recurred after a period of relative freedom. The purpose of the investigation was to try to find some correlation between the type of symptoms presented and the eventual outcome which would be useful for prognostic purposes, but in spite of extensive examination of the results it was not possible to reach any firm conclusions.

The author suggests that further long-term investigations of this nature would be of value for control purposes in the study and evaluation of anticoagulant therapy.

J. B. Wilson

100. **Coronary Arteriosclerotic Heart Disease in the Younger Age Group: Its Greater Frequency in This Group among an Increasingly Older Necropsy Population**
O. SAPHIR, L. OHRINGER, and H. SILVERSTONE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 494–501, May, 1956. 3 figs., 3 refs.

Having observed in recent years an apparent increase in the incidence of arteriosclerotic heart disease (A.H.D.) in the younger age groups, the authors studied the necropsy records at the Michael Reese Hospital, Chicago, covering a period of 34 years. All cases of coronary arteriosclerosis or atheromatosis with or without myocardial fibrosis or infarction in patients over the age of 20 were included, except those in which there were minimal changes. The necropsy records for 3 different periods, 1920–39, 1940–9, and 1950–3, were studied, the incidence of A.H.D. being as follows: 31% of 2,696 necropsies in 1920–39; 31·8% of 2,764 necropsies in 1940–9; and 28·7% of 1,572 necropsies in 1950–3.

Altogether 2,165 patients had A.H.D., 1,403 being males. The proportion of these patients under the age of 50 rose from 7·3% in 1920–39 to 12·2% and 11·5% in 1940–9 and 1950–3 respectively, the greatest increase being in patients aged 40 to 49. Nevertheless, the total number of cases of A.H.D. found at all necropsies did not rise, and the total number of necropsies performed on patients under the age of 50 fell considerably. The authors therefore consider that these figures indicate a significant increase in the number of cases of A.H.D. in the younger age groups; in their view this increase may be related to factors other than diet.

Francis Page

101. **The Application of an Induced Bronchial Collateral Circulation to the Coronary Arteries by Cardiopneumonopexy. I. Anatomical Observations**
J. L. KLINE, H. STERN, W. E. BLOOMER, and A. A. LIEBOW. *American Journal of Pathology* [*Amer. J. Path.*] **32**, 663–693, July–Aug., 1956. 12 figs., bibliography.

102. **Diagnostic and Prognostic Significance of Eosinopenia in Acute Myocardial Infarction**
K. KIRKEBY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 50–56, July, 1956. 2 figs., 13 refs.

The significance of eosinopenia in acute myocardial infarction was studied in a series of 149 patients seen at the Lovisenberg Hospital, Oslo, and Drammen Hospital, Drammen, Norway. In 144 of these patients the eosinophil count was below 50 per c.mm. for 5 to 48 hours after the infarction. The prognosis was poor when the eosinophil count during this period was below 20 per c.mm. and when the eosinopenia lasted more than 7 days. It is suggested that absence of eosinopenia following myocardial infarction may be accounted for by pre-existing eosinophilia or adrenal failure. Early eosinopenia may accompany many other conditions—for example, pulmonary embolism, congestive failure, and cardiac arrhythmia; it is not, however, a feature of uncomplicated angina pectoris, and its absence may therefore be of some value in differentiating this last condition.

P. Mestitz

103. **Selection for Anticoagulant Therapy in Cardiac Infarction Using the Heparin Retarded Coagulation Time**
A. A. F. PEEL. *British Heart Journal* [*Brit. Heart J.*] **18**, 378–384, July, 1956. 3 refs.

Since 1951 the author, working at the Victoria Infirmary, Glasgow, has used the "heparin-retarded coagulation time" (H.R.C.T.) of Rosenthal (*J. Lab. clin. Med.*, 1949, **34**, 1321; *Abstracts of World Medicine*, 1950, **7**, 360) to determine which patients with myocardial infarction should be treated with anticoagulants, these drugs being given to all those in whom the test showed an H.R.C.T. of under 20 minutes.

From the tabulated results a comparison is made between the mortality among 131 patients seen between 1930 and 1950, none of whom was treated with anticoagulants, and 149 seen since 1951, of whom 96 were selected for treatment as described. The over-all mortality at 6 weeks for all patients first seen within a week of infarction was 19% before 1951 and 22·8% after 1951. However, among 53 patients seen before 1951 with no previous history of cardiovascular disease 11 died, a

mortality of 21%, whereas of 56 such patients seen after 1951 only 5 died, a mortality of 9%. [The incidence of shock in the latter group was significantly lower than in the pre-1951 group (22% compared with 36%) and may explain the lower mortality.] Half of the 56 patients seen after 1951 were found not to need anticoagulants and none of these 28 died. On the other hand in patients with a previous history of coronary disease the author states that the results both of H.R.C.T. testing and of anticoagulant treatment "can only be described as depressing". Thus, among 78 such patients seen before 1951 the mortality at 6 weeks was 18%, whereas among 93 seen after 1951 it was 31%. Neither age, sex, nor presence of shock explains this increased mortality, which was much the same in both untreated and treated patients, so that the high mortality cannot be attributed to the withholding of anticoagulants. The picture at the end of one year, however, was much less gloomy, the mortality in the two groups then being 21·6 and 23·6% respectively, which was comparable with that at one year among patients with previous cardiovascular disease seen before 1951, namely, 23%.

It is concluded that the H.R.C.T. test gives a useful indication of the risk of thrombo-embolism occurring, for such phenomena were commoner, both in the first 6 weeks and in the subsequent year, in patients with a shortened H.R.C.T. The test has also been used in the selection of patients with cardiac ischaemia and angina for prophylactic long-term anticoagulant treatment, with promising results. *J. A. Cosh*

104. **Rupture of the Heart after Myocardial Infarction**
J. F. MAHER, G. K. MALLORY, and G. A. LAURENZ. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 1–10, July 5, 1956. Bibliography.

The incidence of rupture of the heart after myocardial infarction was studied in the records of a total of 1,928 cases coming to necropsy between July, 1952, and June, 1954, at the Boston City Hospital. Evidence of recent or healed myocardial infarction was found in 183 cases and cardiac rupture from this cause in 21 of these. Thus there was cardiac rupture in 11·5% of all cases of recent myocardial infarction coming to necropsy. The majority of the patients were in the older age groups, and in over half of them the rupture occurred in the first 5 days after infarction. The sex incidence was equal, in contrast to the prevalence of myocardial infarction in males.

Rupture was more common in hypertensive patients, especially those who remained hypertensive after infarction, than in patients with normal blood pressure. Exertion during the healing of an infarction was a significant factor in the aetiology of cardiac rupture, but there was no correlation between the incidence of the latter and the use of pressor agents, anticoagulants, or the armchair treatment. Rupture was less common in patients with evidence of an old myocardial infarction or congestive cardiac failure, and in those treated with diuretics, digitalis, or antibiotics.

J. Warwick Buckler

HYPERTENSION

105. **Vasomotor Reflexes in Hypertension.** (Сосудистые рефлексы при гипертонической болезни)
N. N. BRAGINA. *Терапевтический Архив* [*Ter. Arkh.*] **28**, 23–28, No. 4, 1956. 4 figs.

The pulse waves of the radial and temporal arteries were recorded piezometrically and magnified by means of an electroencephalograph in a study at the Second Medical Institute, Moscow, of 88 hypertensive patients and 20 healthy controls. The temporal artery was selected as being the most likely to reflect changes in the cerebral circulation, and the radial artery to represent the state of the systemic circulation. Readings were taken on four occasions: at rest, during mental work, after cooling of an upper limb, and while the patient was holding his breath, the patients being divided into three groups according to the severity of the hypertension. Those with mild hypertension resembled the control group in their piezometric responses to the above stimuli. Moderate hypertension was shown to produce several abnormal responses in arterial pulsation, especially in the relative magnitude of the pulsations in the two arteries. In the third group of patients, with severe hypertension and encephalopathy, pulse-wave response to the stimuli was absent or much reduced.

A. Swan

106. **The Response to Rescinnamine Administered Parenterally and Orally for the Treatment of Hypertension**
R. L. HERSHBERGER, E. W. DENNIS, and J. H. MOYER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 542–557, May, 1956. 4 figs., 7 refs.

Since rauwolfia serpentina was first tried in the treatment of hypertension, certain alkaloids and alkaloidal extracts, in addition to reserpine, have been tested for hypotensive activity. In this paper from Baylor University College of Medicine, Houston, Texas, an evaluation of rescinnamine (the trimethoxycinnamic ester of methyl reserpate) in the treatment of mild to moderately severe hypertension is reported.

The drug was given parenterally to 26 patients and by mouth to 84; the patients were unselected. In the first group of 26 patients blood pressure was recorded at 30-minute intervals for 6 to 24 hours after a dose of rescinnamine varying from 2·5 to 15 mg. It was found that 10 mg. was the optimum dose. Subsequently the pressure responses of a further 20 patients given this dose were studied in detail. A significant hypotensive effect was observed in 18 of the 20 patients, the maximum effect being recorded at 5 to 6 hours. A comparison of the action of rescinnamine with that of reserpine given parenterally indicated that the over-all effect of the two drugs was comparable.

Rescinnamine was given for at least 2 months to the second group of patients and for longer than this to 64 of them. In approximately half there was a significant reduction in blood pressure, the full hypotensive effect being observed within 8 weeks of the start of treatment.

Only those patients with mild hypertension became normotensive.

The authors conclude that the hypotensive action of rescinnamine is comparable with that of reserpine, and administration of the former is accompanied by much the same side-effects as administration of reserpine.

Francis Page

PERIPHERAL ARTERIES

107. **Amnion Implantation in Peripheral Vascular Disease**
E. TROENSEGAARD-HANSEN. *British Medical Journal* [*Brit. med. J.*] **2**, 262–268, Aug. 4, 1956. 16 figs., 8 refs.

In this paper from the Charing Cross Hospital, London, the author reports the treatment of a series of 40 cases of intermittent claudication, 38 of which were due to arteriosclerosis and 2 to thrombo-angiitis obliterans, by the implantation of human amnion into the thigh. This method of treatment was suggested by a chance observation that amnioplasty carried out for the treatment of gravitational ulcers had a beneficial effect on intermittent claudication. The patients, all of whom were men, ranged in age from 36 to 89, the average age being 60. All were placed in Group 1 or 2 in Boyd's classification of intermittent claudication. Symptoms had been present for 6 months or more in all but 7 cases.

Investigations performed before and after treatment included exercise tolerance tests with two different types of ergometer, measurement of the walking distance leading to the onset of pain, oscillometry, radiographs of the leg, determination of skin temperature with a mercury skin thermometer, and the radioactive sodium test, as described by Kety and modified by Walder. This consists in the injection of 30 μc. of radioactive sodium in saline into the calf muscle to a depth of 2·5 cm. from the surface and measurement of its rate of disappearance, at rest and during exercise, by means of a Geiger counter placed over the injection site.

Human amnion was collected immediately after delivery and stored at 0° C. for 5 days before being carefully cleaned on the chorionic side only, to preserve the epithelial layer. After being boiled for 3 minutes 2 pieces of amnion, each measuring 7×5 cm. and rolled into a tight pencil, were implanted deep to the fat overlying the fascia lata under local analgesia. A maximum of 48 hours rest in bed was allowed after operation. The procedure was repeated if there was no improvement. The slightest degree of sepsis resulted in failure, while some amnion implants were presumably ineffective owing to damage to the cellular layer before use.

In 3 patients with dry senile gangrene amnion implantation was followed by advancing wet gangrene which eventually necessitated amputation, and the presence of gangrene is now considered an absolute contraindication to this procedure. The condition of one of the other patients remained unchanged, exercise tolerance was increased in 7, and intermittent claudication disappeared in the remaining 29 even on severe exercise, the follow-up period ranging from 8 months to 3½ years. Clinical improvement was accompanied by a return to normal of the rate of disappearance of radioactive sodium and improved performance in the ergometer tests. In 7 cases the dorsalis pedis pulse returned, while in 14 cases there was a marked increase in the oscillometer readings, though good results were not confined to these cases. In the skin temperature there was an immediate post-operative rise, followed after a month by a fall, which, however, was not accompanied by a recurrence of symptoms. In 6 patients with bilateral disease amnion implantation into one thigh was followed by improvement in both legs, and 2 patients with concurrent Raynaud's phenomenon reported an improvement in that condition also.

In 20 cases certain control procedures were carried out, such as simple incision under local analgesia, subcutaneous injection of 0·5 mg. of histamine, and implantation of amnion which had been denuded of its cellular elements. No improvement whatever was noted in 18 of these cases, though all responded well to implantation of amnion subsequently.

The possible mode of action of amnion implants is discussed and an illustrative case history is reported in some detail.

[This is a most interesting paper, and the results recorded make it clearly desirable that the method described should be tried in other centres.]

H. F. Reichenfeld

108. **Clinical Effects of Azapetine (Ilidar) on Peripheral Arterial Disease**
J. M. STALLWORTH and J. V. JEFFORDS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 840–843, June 30, 1956. 8 refs.

At the Roper Hospital (Medical College of South Carolina), Charleston, 52 patients with peripheral arterial disease were treated with " azapetine ", a dibenzazepine derivative with adrenergic-blocking properties, which was given either orally or intravenously. The oral dose was 75 to 100 mg. daily, and the intravenous dose was 1 mg. per kg. body weight dissolved in 250 ml. of saline and injected very slowly over a 30-minute period. The patients included 11 with vasospastic disease and 30 with arteriosclerotic obliterative disease, the remainder having a variety of embolic and other disorders.

Symptomatic improvement was observed in all but 10 cases and was confirmed by oscillometric readings, skin temperature recordings, and observation of the reflex skin changes on warming and cooling of the extremities.

Azapetine was found to be a potent arterial vasodilator giving prompt relief of acute pain due to vasospastic arterial disease, an immediate response to an intravenous injection being obtained in 7 out of 10 cases. It is also useful in the treatment of the vasospastic element in arteriosclerotic obliterative disease. The pattern of response to azapetine, whether administered orally or intravenously, correlated closely with the clinical response to sympathectomy in this group of patients and may be useful in predicting the probable response to that operation.

Leon Gillis

Haematology

109. **Osteomyelopoietic Dysplasia [Osteomyelofibrosis].** (О клиническом варианте остеомиэлопоэтической дисплазии)
M. S. Dul'tsin, E. Z. Novikova, F. E. Faĭnshteĭn, and I. V. Frinovskaya. *Терапевтический Архив [Ter. Arkh.]* **28**, 51–61, No. 4, 1956. 6 figs., 20 refs.

From the Central Lenin Institute of Haematology and Blood Transfusion, Moscow, 11 cases of osteomyelopoietic dysplasia are described and 4 of them discussed in detail. Of these 4, the condition was chronic in 3 with marked splenomegaly, and in the fourth was subacute, the spleen being barely palpable. Photomicrographs of bone-marrow smears, radiographs of bones, and two electrophoretic curves of the serum proteins are reproduced [the marrow smears rather unsatisfactorily]. In 2 cases there was hyperglobulinaemia and an abnormal serum protein electrophoretic pattern. All 4 cases had one unusual feature in common, namely, a predominance of periosteal sclerosis over endosteal sclerosis. The pathogenesis of the condition is discussed [and the authors' views are well expressed in their choice of a title for the paper. Apparently no histological sections of bone marrow were made and no trephine biopsies attempted.] *A. Swan*

110. **Familial Agammaglobulinaemia**
R. H. Elphinstone, I. G. Wickes, and A. B. Anderson. *British Medical Journal [Brit. med. J.]* **2**, 336–338, Aug. 11, 1956. 12 refs.

From Edmonton Chest Clinic and North Middlesex Hospital, London, the case histories are described of 2 brothers with classic familial agammaglobulinaemia, in which there is a marked lowering of resistance to septic infections. The elder brother (born in 1945) had bronchopneumonia at the age of 2 months, and subsequently suffered from repeated attacks of pneumonia and otitis media, as well as a tuberculous pleural effusion (with a positive Mantoux reaction). In 1955, at the age of 10, the diagnosis of agammaglobulinaemia, which had been suspected because of the recurrent infections, was confirmed by paper electrophoresis of the serum, when the γ-globulin level was found to be 0·05 g. per 100 ml. (normal 0·8 to 1·4 g. per 100 ml.). He was then given continuous chemotherapy with oxytetracycline, 100 mg. four times a day, and subsequently completed his first uninterrupted term at school. He is now receiving injections of gammaglobulin, having been included in the Medical Research Council trial of such treatment for hypogammaglobulinaemia.

The younger brother, born in 1951, had at various times suffered from gastro-enteritis, measles, and syn-pneumonic staphylococcal empyema. At the age of 15 months B.C.G. inoculation produced a transiently positive Mantoux reaction; on re-inoculation in 1954 the Mantoux reaction again became positive. Electrophoretic examination of this patient's serum showed a γ-globulin level of 0·15 g. per 100 ml. He has since had a further episode of pneumonia despite continuous oxytetracycline therapy in the same dosage as his brother.

The serum protein pattern of both parents, the patient's aunts, uncles, and paternal grandparents was examined and found to be normal. In both patients the leucocyte count was low during their acute infections, and the erythrocyte sedimentation rate was persistently low.

Denis Abelson

ANAEMIA

111. **Studies in Sickle Cell Anemia. VII. Blood Volume Relationships and the Use of a Plasma Extender in Sickle Cell Disease in Childhood: a Preliminary Report**
M. E. Jenkins, R. B. Scott, and A. D. Ferguson. *Pediatrics [Pediatrics]* **18**, 239–248, Aug., 1956. 4 figs., 26 refs.

The beneficial effects of blood transfusion on the severe visceral and joint pain which commonly occurs in clinical crises of sickle-cell anaemia appear to result from more than the mere replacement of erythrocytes, for they have also been observed after plasma infusions. In this paper from Howard University College of Medicine, District of Columbia, the authors report the results of an investigation of the total erythrocyte and plasma volumes in 18 negro children with sickle-cell anaemia during crises, and of the effect of whole blood and of a " plasma extender ", consisting of 6% dextran in 5% fructose, on the blood volume and circulating haemoglobin mass. Before treatment the mean plasma volume, as determined by a modification of the T-1428 dye method of Gregersen, was greater in the children with sickle-cell anaemia than in a similar number of normal children (62·6 and 46·9 ml. per kg. body weight respectively). As the mean cellular volumes for the two groups were 18·5 and 30·7 ml. per kg. body weight respectively, the mean total blood volume of the patients with sickle-cell anaemia was slightly greater than that of the controls.

In the 9 patients who received transfusions of varying amounts of whole blood the average increase in total blood volume 24 hours after transfusion was 18·2% of the initial volume, but the increase bore no relationship to the initial blood volume in individual patients (detailed results are tabulated). The concurrent increase in total mass of circulating haemoglobin averaged 61·8%, which was 14·5% more than could be accounted for by the transfusion. Clinical improvement occurred in all the patients. In the 9 patients who received dextran infusions of approximately 25 ml. per kg. body weight the mean increase in total blood volume was 10·3%, while the total haemoglobin mass increased by 10·4%. Clinical improvement was observed within 24 hours in

6 of the 9 patients, and in 3 cases lasted for 3 months. The improvement did not necessarily parallel the increase in blood volume.

In the discussion it is suggested that the amelioration of symptoms following dextran infusion may be the result of its volume-expanding action—as is probably also the case with blood transfusion—which allows erythrocytes trapped in organ depots and small peripheral vessels to be mobilized, but it is also probable that in view of the abnormally high level of total plasma protein in patients with sickle-cell anaemia, dextran infusions may exert a protein-sparing effect in relation to liver function. Although there is a tendency to prolongation of the blood clotting time following dextran infusion, this procedure is free of the hazards of blood transfusion.

A. Ackroyd

112. **Intramuscular Iron Therapy in Anaemia of Pregnancy. Two-year Survey**

J. M. Scott. *British Medical Journal* [*Brit. med. J.*] 2, 635–638, Sept. 15, 1956. 5 figs., 8 refs.

During the past 2 years nearly 600 pregnant patients have been treated with intramuscular iron in the form of "imferon" at the Royal Maternity and Women's Hospital, Glasgow. Of the 300 adequately investigated patients here reviewed, 200 had anaemia during pregnancy, the average haemoglobin (Hb.) level being 8·5 g. per 100 ml.; the level in 156 cases was between 8 and 9 g. and in the remainder below 8 g. per 100 ml. In the majority of cases a test dose of 100 ml. of intramuscular iron was followed by the injection of 250 ml. daily in alternate buttocks, the mean total dose in one week being 500 to 600 mg. The amount of iron given was calculated to raise the Hb. level in the antenatal patients to a minimum of 11 g. per 100 ml. [which to some workers would appear to be rather low for the adequate treatment of pregnant women]; however, on the basis of this dosage 80% of the patients showed a satisfactory response, the average increase in the Hb. level in the first week being 0·77 g. per 100 ml., followed by one of 0·8 g. per 100 ml. in the second week, with diminishing increases in successive weeks. In the 44 patients with more severe anaemia the average increase in Hb. level during the first and second weeks was between 1·1 and 1·2 g. per 100 ml. Some further patients showed no improvement in the first week, but responded later; the peripheral blood in these patients showed signs of an increase in haematopoiesis, such as polychromasia and reticulocytosis, although there was no actual increase in the Hb. level, and it is suggested that this could be accounted for by changes in the blood volume and erythrocyte mass.

A study of the utilization of the iron showed that in the antenatal cases there was an increase of 0·3 g. in the Hb. level for every 100 mg. of iron injected. The study also revealed that the apparent utilization of iron was much less in the heavier patients than in the less heavy. A number of the patients were treated early in pregnancy, but it was found necessary to re-treat the majority of these cases; in all, 39 (19·5%) of the total of 200 cases of anaemia during pregnancy required a second course of treatment. [This may have been owing to the fact that the actual amount of iron given was calculated to raise the Hb. level to only 11·0 g. per 100 ml. and that insufficient additional iron was given to allow for the needs of the foetus and increased blood volume.] As had been noted in a previous study, the apparent utilization of iron was greater in the patients with more severe anaemia.

The other 100 patients were treated after delivery, and showed a very rapid response—as was to be expected, since the majority of them had posthaemorrhagic anaemia and haematopoiesis was probably normal before the haemorrhage. The average weekly increase in Hb. level in these cases was 1·2 g. per 100 ml. in the first week, 1·4 g. in the second week, and 1·2 g. in the third week. A general reaction occurred in only 3 cases; in one it was doubtfully due to the injection of iron, in one it resembled an asthmatic attack in a patient with chronic bronchitis, and in the third case it was more in the nature of collapse without apparent cause.

It is concluded that the results of treatment with imferon were very satisfactory and confirm the earlier reports on this preparation. Except in very stout patients the utilization of the iron is as good as that obtained with saccharated iron oxides given intravenously. Certain precautions, however, are necessary: it should first be established that the patient is suffering from a simple iron-deficiency anaemia, and that there are no complicating factors such as infection affecting haematopoiesis. It is also inadvisable to treat any patient giving a history of asthma or of allergic skin rashes.

R. F. Jennison

113. **Absorption, Elimination and Excretion of Orally Administered Vitamin B_{12} in Normal Subjects and in Patients with Pernicious Anemia**

M. Pollycove and L. Apt. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 207–212, Aug. 2, 1956. 4 figs., 20 refs.

In a study carried out at Tufts University School of Medicine, Boston, on normal subjects and patients with pernicious anaemia three methods of determining the degree of absorption of orally administered vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt (^{60}Co) were compared, these being (1) measurement of faecal elimination of the vitamin, (2) measurement of its urinary excretion, and (3) determination of the amount of ^{60}Co deposited in the liver.

Since it was found that the three methods gave reasonably comparable results, the choice of method depends on the technical advantages and disadvantages of their respective procedures. Method 1 requires a 10-day collection of the faeces and entails considerable co-operation from the patient and much inconvenience. There is also the difficulty of ensuring that all stools are in fact collected. As the upper limit of excretion of the vitamin in normal subjects is not far removed from the lower limit in patients with pernicious anaemia the omission of a single critical stool in a case of pernicious anaemia could easily lower the amount of cyanocobalamin recovered to within the normal range. Method 2

(urinary excretion) gives quick results, the specimens are easy to collect, and the normal and pathological ranges are well separated. The method needs, however, a massive " flushing dose " of cyanocobalamin given intramuscularly, and this means that further studies in a case of pernicious anaemia are precluded; also, the method cannot be used for measuring the absorption of an orally administered dose of the vitamin. Method 3 (hepatic deposition) seems to be the easiest. The concentration of ^{60}Co in the liver reaches a maximum in one week and remains constant for some time afterwards—the liver appears to be the only major site of deposition. No collection of excreta is needed, and the only disadvantage is that the result cannot be ascertained for a week; also, if comparison between the effects of orally and parenterally administered cyanocobalamin is required, a second week must elapse before this result can be read. The hepatic deposition method has, in the authors' hands, given results comparable with those of the other two methods and should be easily adaptable to determining the activity of fractions thought to contain the intrinsic factor of Castle. The method requires the use of only a very small dose of radioactive cyanocobalamin (0·5 μg.). *M. C. G. Israëls*

114. **The Effect of Vitamin B_{12} on the Red Cell Size in Pernicious Anaemia**
J. F. Adams. *Scottish Medical Journal* [*Scot. med. J.*] 1, 227–230, July, 1956. 22 refs.

A controlled study of red cell morphology in 17 cases of pernicious anaemia in therapeutic remission is presented. No abnormality in the red cell size was found. It is concluded that vitamin B_{12} [cyanocobalamin] corrects the red cell macrocytosis of pernicious anaemia. —[Author's summary.]

115. **Treatment of Megaloblastic Anaemia of Pregnancy and the Puerperium with Vitamin B_{12}**
E. B. Adams. *British Medical Journal* [*Brit. med. J.*] 2, 398–400, Aug. 18, 1956. 24 refs.

The treatment of 2 African and 8 Indian patients with anaemia of pregnancy is described in this report from the University of Natal, Durban, South Africa. In 6 of these cases bone-marrow smears showed megaloblasts of Ehrlich, those in the 4 others showed megaloblasts of intermediate type, while in all cases giant metamyelocytes were present.

After a control period of 4 to 7 days vitamin B_{12} (cyanocobalamin) was given intramuscularly in a single dose of 100 μg. or in a dosage of 100 μg. daily for 14 days. Of 7 patients treated post partum, the response was as satisfactory in the 3 given the single dose as in the 4 given the larger dosage (1,400 μg.). Of the other 3 (antepartum) cases the response was very unsatisfactory in 2 and there was no response at all in the third. In a further series of 14 similar cases (not described in detail) better responses followed the administration of folic acid; all of these were postpartum cases. In view of these findings it would seem that there may be several varieties of megaloblastic anaemia associated with pregnancy. *R. B. Thompson*

116. **Gastric Biopsy in the Megaloblastic Anaemias**
J. L. Markson and W. M. B. Davidson. *Scottish Medical Journal* [*Scot. med. J.*] 1, 259–266, Aug., 1956. 6 figs., 31 refs.

From Stobhill General Hospital, Glasgow, a study is reported of the histological appearances in gastric biopsy specimens from 16 patients with pernicious anaemia, half of whom had been treated for many years and half were untreated, 42 with iron-deficiency anaemia, 4 with megaloblastic anaemia of pregnancy, 4 with megaloblastic anaemia and steatorrhoea, and 31 controls. The histological appearances were graded as normal, superficial gastritis, atrophic gastritis, or gastric atrophy. Atrophic gastritis was present in 2 of the 16 patients with pernicious anaemia, 14 of the 42 with iron-deficiency anaemia, and 3 of the controls; it was also found in 11 out of 24 additional patients with histamine-fast achlorhydria associated with conditions other than pernicious anaemia. Gastric atrophy was present in 14 of the patients with pernicious anaemia, 4 with iron-deficiency anaemia, 4 controls, and 7 patients with histamine-fast achlorhydria. Since the diagnosis of atrophic gastritis depends on the presence of inflammatory infiltration and fibrosis right down to the muscularis mucosa, the authors conclude from these findings that the state of the gastric mucosa in pernicious anaemia is an end-result of recurrent gastritis, and that the familial or constitutional predisposition in pernicious anaemia is towards recurrent gastritis, which may lead in the end to the complete picture of glandular atrophy.

The detailed histological changes in the 16 cases of pernicious anaemia were as follows. Glandular atrophy was present in all, intestinal metaplasia in 10, marked inflammatory changes in 2, and less marked inflammatory changes in 4. Thickening of the muscularis mucosae was observed in 2 of the 12 biopsy specimens in which this tissue could be examined. Argentaffin cells were present in all 16 cases; oxyntic cells were absent from 13 and zymogenic cells from 10. The gastric mucosa was normal in all except one of the patients with megaloblastic anaemia due to pregnancy or steatorrhoea.

Discussing the complications of gastric biopsy, the authors state that in a series of 111 biopsies haematemesis severe enough to call for blood transfusion developed on 2 occasions; they conclude that as a routine diagnostic procedure the examination carries more risks and yields only slightly more information than the augmented histamine test. *John Naish*

117. **Results of Splenectomy in Auto-immune Haemolytic Anaemia**
G. Chertkow and J. V. Dacie. *British Journal of Haematology* [*Brit. J. Haemat.*] 2, 237–249, July, 1956. 6 figs., 18 refs.

The results of splenectomy in treatment of auto-immune haemolytic anaemia are reported from the Postgraduate Medical School of London. In all 28 patients chosen for study the response to the direct antiglobulin (Coombs) test was positive. The " idiopathic " form of the disease was present in 21, while in 7 the haemolytic disorder was associated with chronic lymphatic leuk-

aemia, lymphosarcoma, or reticulosarcoma. In all except one of the patients splenectomy was performed when the haemoglobin level was falling, in spite of blood transfusion. Haemolytic anaemia had been present for a few months to 5 years. The response to splenectomy was good in 6, fair in 8, and poor in 11; in the other 3 cases the effect was difficult to assess. Of the 21 patients with idiopathic disease, 4 died within months of the operation and one died in relapse almost 6 years after. Two of the patients who responded well had chronic lymphatic leukaemia. Of the 7 patients with secondary haemolytic anaemia, 3 died soon after splenectomy and a fourth died after 18 months. The follow-up period ranged from 6 months to 8 years.

No relationship was found between the response to splenectomy and age, sex, duration of the anaemia, mode of onset, blood picture, the type of antibody—whether warm or cold agglutinins—or size or histological appearances of the spleen. The relatively poor results are ascribed to the production of some auto-immune antibodies and to the destruction of affected erythrocytes elsewhere than in the spleen.

It is concluded that administration of ACTH or cortisone is the treatment of choice in auto-immune haemolytic anaemia, but that splenectomy should be advised if the patient fails to respond to hormone treatment, if prolonged treatment is required, or if repeated blood transfusions are necessary. *T. B. Begg*

LEUKAEMIA

118. **The Antigenic Properties of Endogenous Blastomagenic Substances in the Tissues of Subjects Dying from Leukaemia.** (К вопросу об антигенных свойствах эндогенных бластомогенных веществ из тканей больных, умерших от лейкоза)
M. O. RAUSHENBAKH. *Архив Патологии* [*Arkh. Patol.*] **18**, 50–54, No. 1, 1956. 11 refs.

Specific antigens can be demonstrated in extracts of the tissues and urine of leukaemic patients by repeated injection into rabbits, with the production of anaphylactic reactions and immune bodies against them. The antigen is contained in the benzol-extracted fraction. *L. Crome*

119. **Early Experience with p-(N:N-Di-2-chloroethyl)-aminophenylbutyric Acid (CB 1348), a New Chemotherapeutic Agent Effective in the Treatment of Chronic Lymphocytic Leukemia**
S. J. ALTMAN, A. HAUT, G. E. CARTWRIGHT, and M. M. WINTROBE. *Cancer* [*Cancer (Philad.)*] **9**, 512–517, May–June, 1956. 1 fig., 18 refs.

In this paper from the University of Utah College of Medicine and the Salt Lake County General Hospital, Salt Lake City, experience with " CB 1348 " (*p*-(N-N-di-2-chloroethyl)-aminophenylbutyric acid) in the treatment of 8 patients with chronic lymphocytic leukaemia is reported. The drug was generally prescribed in a dosage of 0·1 mg. per kg. body weight per day. A total amount of 4 to 8 mg. was taken in one dose before breakfast, but higher daily doses were divided and given before meals throughout the day in order to prevent gastro-intestinal disturbances. This treatment resulted in a fall in the leucocyte count, a reduction in the size of enlarged organs, and considerable subjective improvement. The authors state that the drug did not elicit a consistently favourable haemoglobin or platelet response. It appeared, however, to have a satisfactory margin of safety; although gradual depression of cellular elements occurred, this was reversed when administration was interrupted. In the one case in which maintenance therapy was attempted, however, marked granulocytopenia developed, accompanied by a fall in the haemoglobin level; treatment in this case was discontinued because it appeared probable that serious bone-marrow depression might result. *I. M. Rollo*

120. **Myleran Therapy in Malignant Neoplastic Disease; Use of 1:4-Dimethanesulfonyloxybutane with Emphasis on Chronic Granulocytic Leukemia**
G. A. HYMAN and A. GELLHORN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 844–849, June 30, 1956. 6 figs., 18 refs.

The response to busulphan (1:4-dimethanesulfonyloxybutane; " myleran ") of 21 patients with chronic granulocytic leukaemia and 20 with other neoplastic diseases is discussed in this paper from the Francis Delafield Hospital and the Columbia–Presbyterian Medical Center, New York. With a daily dosage by mouth of 2 to 20 mg. remissions lasting up to 48 months were induced in 17 patients with granulocytic leukaemia. The recommended dosage is 10 mg. daily until the leucocyte count falls to 25% of the initial level or until the fall in the leucocyte count ceases, the drug then being discontinued so long as improvement is maintained.

In one group of 9 patients there was a good response, with a rapid fall of the leucocyte count and continued remission after cessation of treatment. In a second group of 8 patients the remission was less complete, a higher and more prolonged dosage and maintenance doses of 2 to 6 mg. daily being required. The 4 patients who failed to respond included one with subacute granulocytic leukaemia. Major toxic reactions included excessive bone-marrow depression with thrombocytopenia and a tendency to haemorrhage, and hyperuricaemia leading to renal damage. The authors state that a blood uric acid level of more than 10 mg. per 100 ml. may be noted when there is rapid destruction of granulocytes, and that a fluid intake of 3 to 4 litres a day may be necessary to overcome this. No beneficial effect was observed in patients with myelomatosis, lymphosarcoma, or carcinoma. Busulphan is considered to be effective in controlling chronic granulocytic leukaemia, but constant haematological supervision is necessary. Whether busulphan therapy is superior to irradiation has yet to be determined. *Kenneth Gurling*

121. **Myleran in the Treatment of Chronic Myeloid Leukaemia.** [In English]
H. B. W. GREIG. *Acta haematologica* [*Acta haemat. (Basel)*] **16**, 171–180, Sept., 1956. 17 refs.

Respiratory System

122. **Mycotic Infections Arising in the Lungs as a Result of Administration of Antibiotics.** (О грибковых поражениях, возникших в результате применения антибиотиков)

V. S. GASILIN and N. A. FILIPOVICH. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **34**, 61–63, No. 7, July, 1956. 1 fig., 2 refs.

The authors, working at the Kuybyshev Medical Institute, encountered 6 patients whose sputum contained the yeast-like organism *Candida albicans*. In 4 of these patients there were symptoms of "candidomycosis", marked by general weakness, severe sweats, cough with mucopurulent sputum, febrile episodes, and occasional haemoptysis. In all the cases *Candida* was obtained from the sputum and grew in pure culture. In all patients radiography revealed increased lung markings, enlarged root shadows, and in one case scattered irregular opacities. The mycotic infection occurred as a complication of a severe illness, such as lymphosarcoma, rheumatism, lung abscess, or bronchiectasis, and followed treatment with penicillin. It diminished, or even cleared, shortly after withdrawal of the penicillin; it appeared also that the administration of sulphonamides or streptomycin had an additional beneficial effect.

In 2 other patients, with chronic lung abscess, *C. albicans* was isolated from the sputum although there were no general symptoms of candidomycosis, suggesting that the organism here was saprophytic; but even in these patients it appeared only after a long course of penicillin and following contact with other cases already infected with the fungus. The authors suggest that *Candida* becomes parasitic as a result of the diminution of the defensive powers of the body during a severe illness together with interference in vitamin metabolism and helped by prolonged administration of antibiotics. They conclude that, although so far there is no proof of cross-infection, it would appear advisable to prevent the contact of debilitated patients with others infected with *Candida*.

Marcel Malden

123. **The Value of Bronchography in Diagnosing "Peripheral" Primary Lung Carcinoma**

C. L. N. ROBINSON and V. G. PECKAR. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 205–209, July, 1956. 8 figs., 18 refs.

An analysis of the last 250 cases of bronchial carcinoma treated at St. Charles's Hospital, London, showed that bronchoscopy had been of no help in diagnosis in 35 (37%) of 94 cases subsequently found inoperable on thoracotomy, in 51 (46%) of 111 treated by pneumonectomy, and in 37 (82%) of 45 treated by lobectomy. In view of this evidence that other methods must be found to facilitate the diagnosis of early lesions, and of the work of Walter and Pryce (*Thorax*, 1955, **10**, 117; *Abstracts of World Medicine*, 1956, **19**, 94) indicating that a high proportion of bronchial tumours are peripheral in origin, the authors now perform bronchography in cases of bronchial carcinoma in which bronchoscopic findings were negative and claim that this procedure has been "diagnostic in over 90% of tumours". [The total number of cases so examined is not stated.]

In the presence of a "peripheral" growth (that is, one beyond bronchoscopic vision) the bronchogram is stated to show one of the following patterns: (1) an abrupt arrest—transverse or oblique, smooth or irregular, concave or convex; (2) a "rat-tail" defect; (3) a lateral irregular defect; or (4) a missing branch. The first two appearances must be differentiated from the longer, smooth obstruction seen in the so-called middle-lobe syndrome. A defect can be regarded as significant only when all other segmental bronchi are properly filled to the periphery of the lung (and when the defect is in the region of the segmental shadow seen on the plain film); proper bronchial filling should therefore be secured at the time of bronchography. [Experienced scrutiny of the bronchograms is equally important if misleading results are to be avoided.] Blockage of a bronchus due to neoplasm can be distinguished from that due to "retained secretions" (as in suppurative pneumonitis) by the fact that the latter gives rise to apparent blocks in several segmental bronchi, whereas the former is strictly localized. Bronchography is also helpful in the differential diagnosis of unresolved or slowly resolving pneumonia when bronchoscopy has been negative, for the bronchi fill to their termination in uncomplicated cases, but show "abrupt arrest" in the presence of obstruction.

The authors conclude that bronchography should supplement bronchoscopy without delay in the investigation of a suspicious peripheral pulmonary shadow. The risk that residual contrast medium may interfere with subsequent radiography does not exist when "dionosil" or a similar preparation is used.

Raymond Parkes

124. **Fifty-one Cases of Lung Cancer with Five-year Survival**

R. H. OVERHOLT and J. A. BOUGAS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 961–963, July 7, 1956. 1 fig.

The factors which determine survival in patients with primary carcinoma of the lung were studied in a series of 51 who were treated at the New England Deaconess Hospital and the Overholt Thoracic Clinic, Boston, before October, 1950, and have survived 5 years or more, one of them for more than 12 years. Of 845 patients seen between June, 1932, and October, 1950, 670 had histologically verified cancer of the lung. Resection was carried out on 234, this group including the 51 who survived 5 years or more. The authors state that age

(the survivors were 24 to 70 years old at the time of operation) and sex (there were six times as many men as women) had little bearing on survival. In 7 cases the lesion was discovered at routine *x*-ray examination of the chest, but in only 4 of these was treatment given within 3 months; the remaining 44 had symptoms—cough, haemoptysis, pain, or other manifestations suggesting persistent respiratory infection. Only 17 patients had physical signs in the chest, but in all 51 the radiographs were abnormal. The average delay before diagnosis was 6·8 months in those surviving compared with 12·2 months in patients who did not survive resection. None of the patients given irradiation or chemotherapy only survived for 5 years.

Pneumonectomy, with removal of mediastinal lymph nodes, was carried out on 48 of the 51 patients, lesser resections being performed on 3. Undifferentiated carcinoma was present in 9 cases, adenocarcinoma in 6, and epidermoid tumour in 36. A similar distribution of growths was observed in the complete series of 670 cases of cancer. In the 5-year survivors the upper lobe was more commonly involved (29 cases) than the lower or middle lobes (16); in 6 cases there was involvement of the main bronchi. The growth was confined to the lung in 34 of the 51 cases, mediastinal lymph nodes being involved in 14 and the chest wall or pulmonary vein in 3. Spread of the growth was observed in a much higher proportion of the patients who did not survive for 5 years. *M. Meredith Brown*

125. **Surgical Management of Neoplastic Pulmonary Metastases**

J. W. STRIEDER. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 1059–1062, June 7, 1956. 7 refs.

The accumulating number of cases of neoplastic pulmonary metastases which have been successfully operated on prompts the author to recommend active surgical measures in the treatment of such cases, since in his opinion a single metastasis, or even multiple lesions, need not be prima facie evidence of widespread dissemination. In this communication from Boston University School of Medicine he reports his operative experience in the treatment of 20 patients on whom 22 resections were carried out, including wedge resection on 2 occasions, segmental resection on 2, lobectomy on 15, and pneumonectomy on 3, the primary tumour being a carcinoma in 17 cases and a sarcoma in 3.

The best results followed the resection of secondary growths from adenocarcinoma of the fundus uteri (2 cases) or bladder (one case) and from hypernephroma (2 cases). It has been reported that the longer the time interval between the appearance of the metastasis after successful removal of the primary tumour, the better the prognosis, but this was not entirely borne out in this admittedly small series. Investigations undertaken to exclude possible multiple dissemination of the disease included total lung tomography, bone-marrow biopsy, radiological studies of the skeleton, and estimation of the urinary acid- and alkaline-phosphatase content. There was one operative death. Of the other 19 patients, 15 survived more than one year following surgical treatment of the lung metastasis, while 8 patients are well and without recurrence one to 8 years after operation.

The author concludes that in a patient whose primary lesion has apparently been successfully removed and in whom a solitary pulmonary metastasis appears which is so located that resection is possible, and provided there is no demonstrable extrapulmonary spread, resection of the growth in the lung should be considered; in certain cases also a palliative operation for the control of haemorrhage or suppuration, though without hope of cure, may be justified. *C. A. Jackson*

126. **The Significance of Selection in Prospective Investigations into an Association between Smoking and Lung Cancer**

R. KORTEWEG. *British Journal of Cancer* [*Brit. J. Cancer*] **10**, 282–291, June, 1956. 4 refs.

127. **Environmental Causes of Cancer of the Lung Other than Tobacco Smoke**

W. C. HUEPER. *Diseases of the Chest* [*Dis. Chest*] **30**, 141–159, Aug., 1956. 5 figs.

128. **Comparative Evaluation of Radioactive Colloidal Gold and Nitrogen Mustard in the Treatment of Serous Effusions of Neoplastic Origin**

F. J. BONTE, J. P. STORAASLI, and A. S. WEISBERGER. *Radiology* [*Radiology*] **67**, 63–66, July, 1956. 1 fig., 17 refs.

Intracavitary therapy with radioactive colloidal gold (^{198}Au) is an accepted method of treatment for malignant effusions, but it has certain disadvantages: (1) it is costly; (2) careful planning is necessary because of the short half-life of ^{198}Au; (3) the amount of radioactivity involved necessitates protection of nursing personnel and makes nursing difficult; and (4) there is a distinct radiation hazard to persons administering the treatment. Nitrogen mustard on the other hand is not costly and there is no hazard to personnel or to the patient if it is used in proper dosage. A single injection of 0·4 mg. per kg. body weight in 50 to 100 ml. of saline is recommended. Excess fluid should be aspirated, and the flow of fluid within chest or abdomen must be free, since nitrogen mustard in a loculated pocket may cause necrosis. The patient's position should be changed every 10 to 15 minutes to ensure even distribution. After 24 hours a further aspiration is necessary to remove free nitrogen mustard and excess fluid.

Of 22 patients with serous thoracic effusions of neoplastic origin treated with radioactive colloidal gold at the University Hospitals, Cleveland, Ohio, 15 were improved and 7 were not improved, while of 38 cases of ascites so treated, 22 were improved. With nitrogen mustard therapy, of 30 cases of thoracic effusion, 18 were improved, and of 10 cases of ascites, 7 were improved. Of 12 patients treated by combined ^{198}Au and nitrogen mustard therapy, 7 were improved.

Nitrogen mustard thus appears to be of the same order of effectiveness as radioactive colloidal gold in the treatment of neoplastic effusions. *I. G. Williams*

Urogenital System

129. **Chronic Pyelonephritis**
J. BROD. *Lancet* [*Lancet*] **1**, 973–981, June 23, 1956. 21 figs., 16 refs.

Since 1948, 132 cases of chronic pyelonephritis have been diagnosed clinically at the Institute for Cardiovascular Research, Prague. Out of 22 cases which were examined by renal biopsy or at necropsy, confirmation of the diagnosis was obtained in 20, while in a parallel clinico-pathological correlation, confirmation was obtained in 49 out of 54 cases diagnosed clinically as glomerulonephritis and in all of 16 cases diagnosed clinically as nephrosclerosis. Of the total series, 44% had a history of frequency of micturition and dysuria and 64% complained of pain in the loins, more frequently dull than colicky; 17% were referred to the clinic because of the chance discovery of proteinuria, 8% because of hypertension, and 1·5% because of thirst or polyuria (although 22% admitted to thirst and 11% to polyuria on direct questioning). About 25% had some fever and rather more than this proportion suffered from lassitude and anorexia. In 81% of cases pathogenic organisms were found in the urine, *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus faecalis* being the most frequent. Leucocytes formed the greater part of the deposit in 76% of the cases (compared with 14% in glomerulonephritis and nephrosclerosis). Proteinuria was common, but rarely exceeded 5 g. per day in amount. The number of casts in the urine was much less than in glomerulonephritis.

At all levels of glomerular filtration rate there was greater impairment of concentrating ability in the patients with pyelonephritis than in those with glomerulonephritis—hence polyuria tends to be more severe in pyelonephritis—and dilution was frequently less impaired than concentration. When urine was collected separately from each kidney and the urine: plasma ratios for creatinine compared, there were far greater differences between the two kidneys in pyelonephritis than in glomerulonephritis or nephrosclerosis. Characteristic radiological findings in pyelonephritis were asymmetry in size and density of the two kidneys, and lack of tone and contraction in the calyces and pelves. There was a causal relationship between pyelonephritis and hypertension, the latter developing with increasing frequency as the pyelonephritis progressed, although it was present in some cases with very little diminution of renal function. An important complication of chronic pyelonephritis is malignant hypertension; the incidence of this complication in pyelonephritic hypertension (19·7%) was significantly higher than in essential hypertension (10%) and it tended to occur at an earlier age (41 as compared with 48 years). On the whole, malignant hypertension was associated only with advanced renal damage in pyelonephritis, whereas essential hypertension may become malignant at any level of glomerular filtration or concentrating ability. The treatment of chronic pyelonephritis is briefly discussed and a 10-point therapeutic regimen summarized. *K. G. Lowe*

130. **Studies of the Etiology and Treatment of Acute Renal Failure**
P. N. JOHNSTONE, R. G. STONE, H. C. BURDICK, H. K. B. ALLEBACH, L. F. PATTON, F. E. TULLER, and L. E. ERB. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 491–494, June 9, 1956. 1 fig., 1 ref.

Observations on the circulation of blood through the isolated kidney of the rabbit and of man by means of an artificial heart and lung machine at the University of Kansas showed that the capillary network became relatively impassable to the corpuscular elements of heparinized whole blood soon after the removal of the kidney from the body, although plasma could be made to circulate freely. It is postulated that this was due to a spastic narrowing of the capillaries and it is further suggested that a similar process takes place in acute renal failure in man. Papaverine hydrochloride had a selective spasmolytic effect on the contracted capillaries, and renal failure, if of similar origin, should respond to this drug. In 10 experiments on rabbit kidneys the average maximum perfusion rate for whole blood was 2·56 ml. per minute, for plasma 7·4 ml. per minute, and for whole blood with added papaverine 20·45 ml. per minute. In 2 experiments with human kidneys—removed 125 and 130 minutes post mortem respectively—comparable increases in the perfusion rate for whole blood were seen after adding papaverine, but in experiments in which more time had elapsed between death and the start of the perfusion no such increase occurred.

Papaverine was used clinically in the treatment of acute renal failure after surgical shock in 4 patients fatally ill from various causes. All 4 benefited as expected from the administration of the drug, either by mouth or by intramuscular injection, in 2-hourly doses of 32 mg., the urinary output increasing greatly and the blood non-protein nitrogen level falling considerably. Similarly impressive results were obtained in 6 other patients who were not fatally ill, all recovering from the acute renal failure within 24 to 120 hours.
L. H. Worth

131. **The Influence of Acute Renal Failure on Resistance to Infection. An Experimental Study**
H. H. BALCH and J. R. EVANS. *Annals of Surgery* [*Ann. Surg.*] **144**, 191–197, Aug., 1956. 8 refs.

132. **Pulmonary Congestion and Edema in Uremia**
S. W. DEPASS, J. STEIN, M. H. POPPEL, and H. G. JACOBSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 5–9, Sept. 1, 1956. 6 figs., 12 refs.

Endocrinology

THYROID GLAND

133. **Clinical Experience with Carbimazole (1-Methyl-2-carbethoxy-thio-imidazole) in the Treatment of Hyperthyroidism**

T. H. McGavack, J. Chevalley, H. K. Reckendorf, and H. O. Haar. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **16**, 887–893, July, 1956. 16 refs.

Carbimazole was given in doses of 15 to 60 mg. daily to 41 patients suffering from hyperthyroidism. The first signs of improvement in the thyrotoxic state were noted from 4 to 21 days after treatment started. Of the 28 patients in whom carbimazole was the definitive medical treatment, 16 were apparently well after a period of more than 4 months without the drug, following courses of treatment varying in duration from 112 to 459 days. A few patients (5%) experienced mild side-effects, such as a facial rash and oedema of the eyes and ankles. It is stated that, clinically, carbimazole and methimazole are about equally effective as antithyroid drugs and some ten times more active than propylthiouracil.

The authors conclude that carbimazole is an effective, relatively safe antithyroid drug which does not markedly increase the already existing hyperplasia of the gland.

G. B. West

134. **Hypothyroidism. Its Aetiology and Relation to Hypometabolism, Hypercholesterolaemia, and Increase in Body-weight**

D. N. Baron. *Lancet* [*Lancet*] **2**, 277–281, Aug. 11, 1956. 2 figs., 22 refs.

At the Middlesex Hospital, London, between January, 1946, and June, 1952, the basal metabolic rate (B.M.R.) was estimated in over 10,000 patients, 227 of whom were hypometabolic (B.M.R. below −25%), 119 of these being clinically hypothyroid. The hospital records revealed a further 21 hypothyroid patients whose B.M.R. was not determined or was above −25%. These 140 cases of clinical hypothyroidism are analysed in this paper.

In 93 patients (15 males and 78 females), including cretins, the hypothyroidism was idiopathic, the age at onset in over half of these being 40 to 60 years (mean 45 years). These cases represented 0·07% of the total hospital admissions in the period under review. Hypothyroidism followed thyroidectomy in 31 cases (4% of the total number of thyroidectomies performed at the hospital). This incidence was independent of sex and the type of goitre, and was not related to the amount of lymphoid tissue in the excised gland. In 2 cases hypothyroidism was noted after acute thyroiditis, and in one case 15 years after iodine treatment for Graves's disease. It was associated with the use of antithyroid drugs in 4 cases (for heart disease in one and for hyperthyroidism in 3). In 6 cases hypothyroidism followed irradiation of the neck (one case each of Hashimoto's disease and Riedel's disease, 3 of thyrotoxicosis, and one of tuberculous cervical adenitis). Finally, treatment with radioactive iodine preceded hypothyroidism in 3 cases (12% of all cases so treated in the period under review).

In most of the patients the B.M.R. was between −25% and −35% (mean −30·6%). It was lower (mean −31·6%) in the idiopathic cases than in those with hypothyroidism due to external causes (mean −28·3%), probably because there had been better medical supervision in the latter. However, hypothyroidism may occur with a normal B.M.R.; in this series the B.M.R. was above −20% in 5 patients and between −20% and −25% in 12 (8%). The serum cholesterol level was raised in 58 out of the 65 cases in which this was estimated, the mean being 398 mg. per 100 ml. (normal value 140 to 260 mg. per 100 ml.). No correlation was found between the serum cholesterol level and the B.M.R.

It was shown statistically that as a group the patients were overweight, but the excess of weight (mean 10·9 lb. (4·9 kg.)) bore no relation to the B.M.R. After treatment the mean loss was 5·4 lb. (2·45 kg.). It is suggested that the weight gain arises from an increase in myxoedematous tissue and water and not in body protein.

A. Gordon Beckett

135. **The Effect of Thyroid Disease on Calcium Metabolism in Man**

S. M. Krane, G. L. Brownell, J. B. Stanbury, and H. Corrigan. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 874–887, Aug., 1956. 6 figs., 25 refs.

The effect of disorders of the thyroid gland on calcium metabolism in man was studied at Massachusetts General Hospital (Harvard Medical School), Boston, by the use of radioactive calcium (^{45}Ca) and the isotope dilution technique in groups of euthyroid, hyperthyroid, and hypothyroid patients, comparison being made with euthyroid patients with hypoparathyroidism and with Paget's disease. The isotope was administered by intravenous injection in doses of 5 to 7 μc., and total values and specific activities in the serum, urine, and faeces were determined, together with the performance of balance studies of stable calcium, phosphorus, and nitrogen. (The detailed results are presented in tables.)

Semi-logarithmic plotting of the specific activities in the urine and serum against time after administration indicated that the curves could be resolved into three exponential functions, probably representing three discrete calcium compartments. It is suggested that these are the extracellular fluid, the surface of bone crystals, and the interior of bone crystals. The findings showed that there was a rapid reversible flow of calcium between

the three compartments, the rates of flow being sensitive to changes in thyroid function. In patients in negative calcium balance the calcium lost from the extracellular fluid by excretion was replaced by the transfer of calcium from bone.

In the hyperthyroid patients, all of whom were in negative calcium balance, there was a more rapid decline of specific activity in the serum and urine and an increase in the dimensions of the three calcium compartments accompanied by an increased rate of exchange, as compared with euthyroid control subjects. These findings indicate that there is an increased rate of osteogenesis as well as increased bone resorption, so that in hyperthyroidism excessive destruction of bone may be the primary event. The reverse was seen in the myxoedematous patients, in whom there was a reduction in the rate of fall of specific activities and in the dimensions of, and rate of exchange between, the calcium compartments. The findings in euthyroid patients with Paget's disease of bone were analogous to those in the hyperthyroid patients. *F. W. Chattaway*

136. **Diagnosis and Treatment of Thyroiditis**
J. W. HENDRICK. *Annals of Surgery* [*Ann. Surg.*] **144**, 176–187, Aug., 1956. 3 figs., 9 refs.

137. **Mental Disorder Associated with Thyroid Dysfunction**
I. GREGORY. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **75**, 489–492, Sept. 15, 1956. 21 refs.

PITUITARY GLAND

138. **Acquired Resistance to Corticotropins**
H. F. WEST. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 124–133, June, 1956. 14 figs., 13 refs.

In the course of a study of the long-term treatment of severe rheumatoid arthritis and ankylosing spondylitis with corticotrophin (ACTH) started at the Sheffield Rheumatism Centre 3 years ago it was observed that in many cases highly purified preparations of corticotrophin slowly lost the ability to stimulate the adrenal cortex. All the 51 patients studied responded well initially, but 42 eventually became resistant, 12 of them to 3 or more different preparations. The degree of adrenocortical stimulation was measured by assay of the 17-ketogenic steroids or 17-hydroxycorticosteroids in 24-hour specimens of urine. Since more than 1,000 steroid assays were carried out the results could not be presented in detail, but those in a number of individual cases are depicted graphically.

The author considers that the loss of effectiveness of corticotrophin was due to an acquired resistance, since there was no evidence of exhaustion of the adrenal cortex, and all the preparations were effective in previously untreated patients. The nature of the acquired resistance is, however, unknown. Several workers have demonstrated the production of circulating antibodies against the early, relatively crude preparations of corticotrophin, but similar findings have not been reported with the highly purified preparations. The author considers it unlikely that the pure hormone is itself allergenic in view of the specific nature of the acquired resistance and because 2 of the most sensitive patients studied responded well to Dixon's corticotrophin A_1, which is thought to contain no contaminating protein.

However, local allergic reactions at the site of injection occurred in 17 patients and general reactions were also thought to have occurred in a number of cases, though this was not certain because the symptoms were hard to distinguish from those of the primary disease, which relapsed when allergenic injections were given repeatedly. The author concludes that efforts should be made to obtain more highly purified preparations of corticotrophin, and recommends that " a statement as to *purity*, measured in a recognized unit per mg. protein solid, should accompany all preparations " of the hormone.
K. C. Robinson

PANCREAS

139. **Effects of Insulin after Adrenalectomy**
J. GINSBURG and A. PATON. *Lancet* [*Lancet*] **2**, 491–494, Sept. 8, 1956. 4 figs., 28 refs.

The object of the investigation here reported from St. Thomas's Hospital, London, was to study the manner and rate of recovery from insulin hypoglycaemia in patients who had undergone bilateral adrenalectomy and who were therefore unable to increase the output of adrenaline. The patients, 9 women and 3 men, all received 25 mg. of cortisone twice a day postoperatively. The insulin tolerance tests, for which 0·1 unit of insulin per kg. body weight was given intravenously, were carried out within 3 weeks of operation and after a 10 to 12 hours' fast. Duplicate samples of 0·05 ml. of capillary blood were drawn before the injection and at 15, 30, 45, 60, 90, and in a few cases 120 minutes after it, and the blood sugar estimated by a modification of the Shaffer–Hartmann method. The blood flow in the hand and forearm was also measured by means of venous occlusion plethysmography. Glucose was given orally as a precaution at the end of the test, although no severe reaction was observed.

General symptoms occurred in all the patients about 30 to 45 minutes after the injection. Inspection of the blood sugar curves showed that the fall in the blood sugar level was maximal at 30 minutes; the level returned to normal values within 2 hours of the administration of insulin. In 2 cases in which the test had also been performed preoperatively little difference was noted in the postoperative curve. It was thus clear that adrenalectomy in man does not impair the capacity to restore the circulating glucose level after the occurrence of hypoglycaemia. This capacity cannot therefore be related to increased output of adrenaline or corticosteroids.

The onset of the hypoglycaemic reaction was associated, as in many normal subjects, with a much increased blood flow in the hand and forearm. The tachycardia and increase in pulse pressure, however, which are

normally encountered in hypoglycaemia (and usually ascribed to adrenaline release) did not occur in these adrenalectomized patients, slight changes only being observed. In the absence of such changes it is suggested that vasoconstriction occurred elsewhere, perhaps in the splanchnic vascular bed. *Denis Abelson*

140. **The Interaction of Glucagon and Insulin on Blood Glucose**

H. ELRICK, C. J. HLAD, Y. ARAI, and A. SMITH. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 757–762, July, 1956. 3 figs., 16 refs.

At the University of Colorado, Denver, the authors have studied the effects of glucagon and insulin on the peripheral utilization of glucose. The two substances were given both together and separately and the effects compared, 12 healthy subjects receiving insulin, 12 glucagon, and 12 both together intravenously; all received intravenous glucose at a constant rate during a preliminary control period and during the infusion of the hormones. All subjects were on a standard high-carbohydrate, high-calorie diet. Estimations of the glucose content of venous and capillary blood were made at intervals of 5 to 10 minutes, a total of 30 to 40 being made during each experiment.

The infusion of insulin alone was followed by a fall in arterial and venous glucose levels to or below fasting levels. Insulin and glucagon together produced in 8 of the 12 subjects a marked arterial hyperglycaemia (over 200 mg. per 100 ml.) with a slight rise in the venous glucose levels; in 3 others there was little or no rise in the arterial glucose level. In 11 of the 12 subjects there was a marked increase in the difference between arterial and venous blood glucose levels. In no case was there a fall below fasting levels. The A-V/A value (arteriovenous glucose difference divided by arterial glucose concentration, taken as an index of peripheral glucose utilization) for insulin and glucagon given together was greater than for either alone. The arterial hyperglycaemia following administration of glucagon and insulin together was often greater than that caused by glucagon alone. It is considered that this may have resulted from higher levels of liver glucagon induced by giving the insulin 15 to 25 minutes before the glucagon.

It is concluded that glucagon and insulin thus jointly enhanced peripheral utilization of glucose and counteracted the opposing effect of each other on the blood sugar level. There were considerable individual differences in response, but these showed no correlation with body weight. *A. Gordon Beckett*

141. **Diabetes of Thirty-five Years' Duration**

H. F. ROOT and P. BARCLAY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 801–806, June 30, 1956. 6 refs.

A review of the records at the Joslin Clinic, Boston, of 34,000 diabetic patients showed that there were 96 whose histories indicated an onset of the disease 35 to 46 years previously—that is, before the discovery of insulin. Of the 96, 45 had died, death being due to coronary arteriosclerosis. In 7 of the 51 survivors diabetes was diagnosed in childhood. Altogether 90 of the patients had had insulin treatment. Of the 51 who received insulin for more than 20 years, 34 were alive, whereas of the 39 who received insulin for less than 20 years, 16 were living and 23 were dead. Interesting statistical details are given in a number of tables.

A. I. Suchett-Kaye

142. **Carbohydrate Metabolism. II. Changes in the Serum Pyruvic Acid during Glucose-tolerance Test in Normals, Diabetics, and Prediabetic Women**

N. SHRIFTER and M. D. KRITZER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **98**, 28–34, July, 1956. 4 figs., 17 refs.

Pyruvic acid is one of the most active compounds concerned in intermediary metabolism, and glucose, by the processes of glycolysis, is one of the major sources of pyruvate in the body. The metabolism of the α-keto acid has therefore been widely investigated in diabetes mellitus because of the underlying disorder of carbohydrate metabolism. Experimental work on diabetic patients, however, has been limited to studies of the variations in the blood pyruvate concentration either in random blood samples or after the administration of glucose and/or insulin, and interpretation of the published results has been difficult because of the lack of specificity of some of the analytical methods used and also because there appear to be several types of diabetes mellitus. The present authors, working at the Los Angeles County General Hospital (University of Southern California), have considered the effect of an additional factor, namely, the route of administration of the glucose. In these studies, therefore, glucose was given orally to 20 normal subjects and to 13 elderly patients with long-standing mild diabetes who required no insulin, and intravenously to 9 normal subjects and 8 mild diabetics, the blood pyruvate level being estimated by the method of Lu (*Biochem. J.*, 1939, **33**, 249).

In the normal subjects the oral or intravenous administration of glucose caused an initial rise in the blood pyruvate content at 1 hour, followed by a gradual fall to the initial value at the end of 3 hours. Similarly, in diabetic patients receiving glucose orally the pyruvate level rose gradually throughout the experimental period of 3 hours, whereas in those given the glucose intravenously the blood pyruvate level fell and was low at both 30 and 60 minutes, rose to the initial level between the first and second hours, and declined again during the third hour. The authors speculate on the various mechanisms which may be involved, such as decreased pyruvate production, increased pyruvate removal, or a shift of pyruvate from the extracellular fluid into the cells, in causing the early fall in blood pyruvate level following the intravenous infusion of glucose in the diabetic patient.

Glucose was also administered orally to a group of women who had given birth to large babies; these were divided into two sub-groups, "prediabetics" (30 patients), in whom the glucose tolerance curve was normal at the time of the experiments, and "recent diabetics" (16 patients) who showed a diabetic type of response to the oral glucose tolerance test. The response

to oral glucose in the prediabetic subjects resembled that of normal subjects in showing a prompt rise in the blood pyruvate level at 1 hour followed by a gradual fall, whereas in the recent diabetics the peak value of blood pyruvate level was reached later than normal, namely, at 2 hours rather than at 1 hour. *M. J. H. Smith*

143. **Action of Butyltolylsulfonylurea on Liver Glycogenolysis**

J. M. TYBERGHEIN, Y. D. HALSEY, and R. H. WILLIAMS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **92**, 322–324, June, 1956. 17 refs.

In experiments carried out at the University of Washington School of Medicine, Seattle, the probable site of action of the hypoglycaemic agent butyltolylsulphonylurea (BTSU) was investigated in rats and rabbits. The former were divided into two groups, the first being fasted for 24 hours and the second fed on glucose for 24 hours, two control groups being similarly treated. Both experimental groups were then given BTSU in a dosage of 80 mg. every 12 hours and killed after the third dose, when blood sugar levels were estimated and liver slices prepared for the determination of glycogen content and examined for glucose-6-phosphatase activity by the estimation of inorganic phosphate in the incubation medium. In the rabbit experiments the procedure was similar, except that larger doses of BTSU were given (500 mg. every 12 hours for 4 days, the first and last doses being 1,000 mg.).

The results showed that the liver glycogen content in the BTSU-treated fasting rats was greater than in the fasting untreated control animals, but was almost the same as in the glucose-fed animals, whether treated with BTSU or not, indicating that the conversion of glucose to glycogen is not significantly impaired by administration of BTSU. Hypoglycaemia was noted in all animals receiving BTSU. The studies *in vitro* showed that the glucose output of liver slices from rabbits given BTSU was less than that of those from control animals, and that the addition of BTSU to the incubation medium *in vitro* did not decrease the glucose output of liver slices from normal animals. It is suggested that the reduction of hepatic glucose output is probably the result of inhibition of glucose-6-phosphatase activity in the liver.

J. N. Harris-Jones

144. **Hypoglycemic Action of Orinase. Effect on Output of Glucose by Liver**

G. E. ANDERSON, A. J. PERFETTO, C. M. TERMINE, and R. R. MONACO. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **92**, 340–345, June, 1956. 4 figs., 6 refs.

The determination at short intervals of the glucose content of blood from the hepatic vein has shown that there is gross and unpredictable irregularity of output of glucose from the liver in the post-absorption period. The authors were able to show that these fluctuations are reflected in the glucose content of femoral arterial blood, and consider it probable that they are due to the effect of glucagon and that they perform the physiological function of stimulating the production and action of insulin in the post-absorption period.

In studies carried out at New York State University College of Medicine, Brooklyn, on dogs subjected to long- and short-term treatment with "orinase" (1-butyl-3-tolyl-sulphonylurea) estimations of the glucose content were made on arterial blood taken at one-minute intervals before and after giving glucagon; finally the animals were subjected to laparotomy, and blood taken direct from the hepatic vein after giving glucagon was examined for glucose concentration. The effects of giving glucagon intravenously together with orinase were also observed. These experiments showed that in addition to the general fall in the mean blood glucose level caused by orinase, the marked fluctuations in the blood glucose content of peripheral arterial blood were also greatly reduced. The response to glucagon was expressed in an exaggerated return of the earlier and apparently normal oscillations. Following the intravenous administration of orinase there was a sharp decline (up to 33%) in the quantitative hepatic glucose output, which appeared after about 10 minutes and was complete within 60 minutes or less. This effect was abolished by subsequent administration of small doses of glucagon, and did not occur at all if glucagon was given simultaneously with orinase.

The authors conclude that the block due to orinase is proximal to the phosphorylase systems in the liver, since it stops fluctuations in glucose output which reflect phosphorylase glycogenolysis. The exaggerated response to glucagon after orinase medication is interpreted as indicating that glucagon production has been suppressed; however, since the authors observed no pathological changes in the alpha cells of the pancreas after prolonged or intensive drug therapy, they assume that this inhibition is functional and reversible, and not anatomical. *J. N. Harris-Jones*

145. **The Oral Treatment of Diabetes with N-(Sulphonyl-*p*-methylbenzene)-N′-*n*-butylurea or "D860" (a Product without Antibacterial Activity).** (Note préliminaire sur le traitement oral du diabète par le N-(sulfonyl *p*-méthylbenzène)-N′-*n*-butyl urée ou D 860 (produit dénué d'action antibactérienne))

R. MOREAU, R. DEUIL, A. SARRAZIN, P. M. DE TRAVERSE, and M. MARTINET. *Presse médicale* [*Presse méd.*] **64**, 1261–1264, July 7, 1956. 6 figs., 1 ref.

This paper reports a clinical trial of the hypoglycaemic sulphonamide sulphonylmethylbenzenebutylurea ("D 860"). The authors point out that D 860 reduces the blood sugar level in normal subjects and in diabetics and, in contrast to "BZ 55" (carbutamide), has no antibacterial action. Their 27 diabetic patients were divided into two groups: (1) patients over the age of 40 who were poorly controlled on diet, but had never had insulin, and (2) patients over 40 who had been diabetic for a fairly long time and had been receiving insulin. Of the 14 patients in the first group, 9 were perfectly controlled by D 860 within a few days and remained so for over 2 months on doses of about 2 g.

daily, 3 were moderately well controlled, and in 2 the treatment failed—but one of these had had diabetes mellitus for 23 years. Of the 13 patients in Group 2, 11 who had previously taken between 15 and 55 units of a depot insulin daily became better controlled on taking 2 g. of D 860 daily, without any insulin. The other 2 cases in this group were failures; these were young, underweight diabetics who had been on insulin for a long time. (Unexpected success was met with in a girl of 16 who had been taking 15 units of protamine zinc insulin daily, and in a woman over 60 who had had 55 units of soluble insulin a day for 20 years.) In both groups of patients, if control was satisfactory, the maintenance dose of D 860 could be reduced to 0·5 to 1 g. daily.

Blood counts, liver function tests, blood urea estimations, and serum electrophoresis were regularly carried out, but no contraindications to the drug were found over a period of 2 months. The drug was not given to patients with renal or hepatic dysfunction, skin lesions, or abnormal blood counts. Like other workers in this field the authors conclude that only prolonged clinical trials with these drugs will reveal their mode of action and degree of toxicity. *Joan Yell*

146. **Serum-cholinesterase Levels in Diabetes Mellitus**
R. H. S. THOMPSON and J. R. TROUNCE. *Lancet* [*Lancet*] **1**, 656–658, May 12, 1956. 1 fig., 25 refs.

At Guy's Hospital, London, the serum cholinesterase level was estimated in 50 adult diabetic out-patients (of whom 25 were obese and 25 non-obese), 25 adult obese non-diabetic patients, and 33 non-obese healthy adults. The cholinesterase activity was estimated manometrically; this method depends on the fact that the free acid released from the choline ester by the action of cholinesterase liberates carbon dioxide from 0·025 M sodium bicarbonate medium, using acetylcholine perchlorate (0·015 M) as substrate. The results are expressed in microlitres (μl.) of carbon dioxide per ml. of serum per minute.

The serum cholinesterase levels in healthy adults ranged from 53 to 102 (mean 76) μl. In 15 of the 25 obese diabetics the values were above this range (108 to 175 μl.), while the mean value in the 25 obese non-diabetic patients (as in the obese diabetics) was significantly higher than in healthy adults, 11 of them (44%) showing values of 105 to 151 μl. Of the 25 non-obese diabetics, 23 (92%) had normal levels, and in none of them did the level exceed 120 μl. Although 2 non-obese diabetic patients gave values above the highest " normal " value observed there was no significant difference between the levels in non-obese diabetics and those in the healthy subjects. But the differences between the levels in non-obese and obese diabetics and between those in obese non-diabetics and the healthy subjects were highly significant. There was no correlation between the serum cholinesterase level and the severity of the diabetes (as estimated by insulin requirements) or the degree of control of the disease.

It is concluded that the elevation of the serum cholinesterase level in diabetics is associated with the accompanying obesity rather than with the diabetes itself. In a discussion of the literature the authors suggest that the pseudocholinesterase present in human plasma and liver (which accounts for the greater part of cholinesterase activity) may be concerned with some aspect of fat metabolism. *Robert de Mowbray*

ADRENAL GLANDS

147. **Chemical and Clinical Problems of the Adrenal Cortex**
F. T. G. PRUNTY. *British Medical Journal* [*Brit. med. J.*] **2**, 615–622 and 673–686, Sept. 15 and 22, 1956. 16 figs., bibliography.

Relevant knowledge of compounds secreted by the adrenal cortex and their metabolism is reviewed. Experiments are discussed which give information about the action of corticotrophin in man. Difficulties in evaluating the response due to variations in the activity of different batches of corticotrophin are stressed. After making due allowance for these difficulties, it is possible to define a " spectrum " of response in individuals with various pathological entities. Particular attention is drawn to the response of patients with idiopathic hirsutism, and the effects are contrasted with those in hypopituitarism and normal childhood on the one hand, and in adrenal cortical virilism on the other. Comparisons are made between the effect of exogenous corticotrophin and the endogenous stimuli produced by surgical trauma.

A condition of " basal hypo-adrenal corticalism " is defined and its significance discussed. The possibility of synergic action between corticotrophin and a factor associated with growth hormone, gonadotrophins, and thyroid hormones is considered. There seems little doubt that thyroid hormones are of great importance in the responsiveness of the adrenals. Evidence concerning the existence of a potentiating factor to corticotrophin for the stimulation of adrenal androgens is shown to be worthy of consideration. A similarity in behaviour of certain adult male obese subjects to that of hirsute women is noted and contrasted with others bearing a superficial resemblance to patients with Cushing's syndrome.

Attention is drawn to clinical problems in relation to alterations of cerebral activity in patients with Addison's disease and hypopituitarism and to difficulties which arise when space-occupying intracerebral lesions may be present. A patient with long-standing encephalitis has been studied, with particular reference to the secondary endocrinological phenomena which ensued, and the significance of these is discussed. Recent advances and ideas in relation to the diagnostic problems in Cushing's syndrome and in patients with adrenal cortical tumours, particularly when hypocalcaemia and renal symptoms are present, are considered and supplemented with additional observations.—[Author's summary.]

148. **Primary Aldosteronism Due to Adrenocortical Hyperplasia**
F. S. P. VAN BUCHEM, H. DOORENBOS, and H. S. ELINGS. *Lancet* [*Lancet*] **2**, 335–337, Aug. 18, 1956. 6 figs., 12 refs.

The Rheumatic Diseases

RHEUMATIC FEVER

149. **Rheumatic Fever. The Use of Serum as Antigen in Skin Tests.** [In English]
B. LANDTMAN. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **2**, 156–161, 1956. 19 refs.

A comparative study of the skin sensitivity to serum of 34 children with rheumatic fever, chorea, or inactive rheumatic heart disease and 166 children with other ailments, mostly non-infectious and unrelated to rheumatic fever, is reported from the University of Helsinki. A drop of serum obtained by centrifuging blood withdrawn within the hour was placed on the skin and a scratch made through it, taking care to avoid drawing blood. A control scratch was made through a drop of saline. A cutaneous reaction—namely, a weal surrounded by erythema which appeared within 10 minutes and faded in 30 minutes—was seen in a number of cases, the result of the test being interpreted as positive when the serum gave rise to this skin reaction and control saline did not. About 10% of the control children gave a positive reaction to sera obtained from controls and from children with rheumatic fever. A similar proportion of children with rheumatic fever gave a positive response to control sera, but the proportion giving a positive response to sera from rheumatic children was much higher, a skin reaction being observed in 60 out of 73 tests. There was no correlation between the result of the test and the treatment given, but the strongest reaction occurred when the test was carried out on children in the acute stage of rheumatic fever with sera from patients in the same stage of the disease.

E. G. L. Bywaters

150. **Comparative Study of Treatment with Hormones and Salicylates in Rheumatic Fever in Children.** (Etude comparée du traitement hormonal et de la salicylothérapie dans la maladie de Bouillaud chez l'enfant)
M. BERNHEIM, R. FRANÇOIS, C. MOURIQUAND, and G. GROS. *Journal de médecine de Lyon* [*J. Méd. Lyon*] 37, 617–623, Sept. 5, 1956.

During 1946 to 1949 inclusive, at the Children's Medical Clinic, Lyons, 88 children suffering from rheumatic fever were treated with salicylates in doses of 5 to 12 g. by mouth daily for 3 to 6 months. In the following 4 years either corticotrophin (ACTH) or cortisone was used in treating 90 similar children. The dose of ACTH varied between 50 and 200 mg. [? units] daily, that of cortisone from 100 to 200 mg. daily, and the duration of treatment from 11 to 150 days, with an average of 30 days; at the end of this course of hormone therapy salicylates were given for another month or two.

In a retrospective review of the results it was considered that the two groups were comparable as regards age and sex incidence, the condition of the heart on admission, the duration of the symptoms before treatment began (18 and 20 days respectively), and the proportion of patients who had had previous attacks. Those treated with hormones have naturally been observed for much shorter periods, but the minimum period of follow-up was fixed at 6 months after the onset of the disease. The authors conclude that the use of hormones represents a great advance in the treatment of rheumatic fever. The clinical progress was more rapid in all respects and toxic phenomena were far less frequent than with salicylates. There were 7 deaths among those treated with salicylates compared with only 2 in the hormone group, although the latter included 17 cases of severe pancarditis while there were only 11 such cases in the salicylate group. There was no difference in the incidence of valvular damage among the survivors in the two groups.

[The conclusions drawn from this study must be accepted with reserve because there was no definite prearranged plan of treatment in either group and the two groups were not treated concurrently.]

John Lorber

CHRONIC RHEUMATISM

151. **Uveitis and Rheumatic Diseases**
A. STANWORTH and J. SHARP. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 140–150, June, 1956. 1 fig., bibliography.

Of 237 patients attending the Out-patient Clinic of Manchester University Department of Ophthalmology with uveitis during a period of 2½ years, 209 in all were examined for coincident rheumatic disease. The uveitis was classified according to the site and type of inflammation and the patients were divided into those with a known non-rheumatic cause for the uveitis (such as herpes zoster ophthalmicus or secondary syphilis) and those without such cause. In the whole series there were 44 patients with osteoarthritis and 22 with rheumatoid arthritis. Moreover, a further analysis did not reveal any significant difference between the incidence of these diseases in patients with and without a known non-rheumatic cause for the uveitis. There were, in addition, 16 patients with Reiter's disease (nearly all having spinal involvement) and 39 with " spinal arthritis ", indicating a special association between these conditions and the uveitis; furthermore, the uveitis was of the unilateral, non-granulomatous, anterior type in nearly every case. Among all the cases of this type of uveitis in the series, the incidence of ankylosing spondylitis (including atypical spondylitis) may have been as high as 49% in males and 35·6% for both sexes. The spinal disease was judged to be inactive in one-third of the patients at the time of development of the eye lesion.

K. C. Robinson

152. **Haemodilution in Rheumatoid Disease**
M. R. JEFFREY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 151–159, June, 1956. 8 figs., 12 refs.

In an investigation carried out at the Royal National Hospital for Rheumatic Diseases, Bath, the plasma volume was estimated in 88 patients with rheumatoid disease and 42 healthy control subjects. The dye-dilution technique was employed, and blood and cell volumes were calculated by means of the haematocrit values. The two groups were comparable in respect of body weight, surface area, and age. The mean plasma volume in relation to weight and surface area was greater for both sexes in the patients with rheumatoid arthritis than in the controls. However, both in controls and patients, there was a tendency for the plasma volume per unit body weight to decrease with rise in weight. Assuming this to be a straight-line relationship, the author found no significant difference between the regression coefficients calculated for the two groups. The mean haemoglobin levels of the male and female patients with rheumatoid disease were 3·8 and 2·6 g. per 100 ml. respectively below those of the male and female controls. Anaemia of this degree has been shown to cause changes in the blood, plasma, and cell volumes, and the author considers that this is an adequate explanation for the differences found. Patients with very active disease, as shown by a high erythrocyte sedimentation rate, did not have a particularly high plasma volume, nor did 13 patients with iron-refractory anaemia. He therefore concludes that " the hypothesis of primary hydraemia, causing haemodilution, appears to be unnecessary ". *K. C. Robinson*

153. **A Specific Substance in the Blood and Joint Fluid in Rheumatoid Arthritis.** (Eine für den chronischen Gelenkrheumatismus charakteristische Substanz im Blute und in der Gelenkflüssigkeit)
N. SVARTZ. *Bulletin der Schweizerischen Akademie der medizinischen Wissenschaften* [*Bull. schweiz. Akad. med. Wiss.*] **12**, 99–118, June, 1956. 3 figs., 12 refs.

Investigations were carried out at Karolinska Sjukhuset, Stockholm, into the nature of the factor present in the blood and joint fluid in rheumatoid arthritis which is responsible for the agglutination of sensitized sheep's erythrocytes in the Waaler–Rose test. Sera which gave a positive haemagglutination reaction were subjected to electrophoresis and the different fractions tested separately. As expected, the factor causing the reaction was found with the gamma-globulin fraction, but did not correspond with any of those normally found in health. Experimental findings suggested that it is a protein body which is probably bound to another radical. Haemoglobin is not involved in the reaction, since it is the stroma of the erythrocytes which becomes " sensitized ".

It was found that a haemagglutinating factor could be produced experimentally in rabbits by injecting serum or synovial fluid from appropriate patients. However, the factor thus produced had only a low haemagglutinating titre and its demonstration was made difficult by the development in the animal of an anti-factor. A haemagglutinating substance was also produced by culturing certain unclassified cocci isolated from the pharynx on connective tissue (joint capsule or tendon), the bacteria-free filtrate having properties similar to those of the serum factor, though it was not possible to prove complete identity. This haemagglutinating factor is probably produced by the enzymic action of the bacteria on the connective tissue, and it is suggested that the factor present in human blood in rheumatoid arthritis is also the product of an abnormal enzymic process involving the connective tissue.

G. W. Csonka

154. **Pilot Study of Intra-articular Procaine and Hydrocortisone Acetate in Rheumatoid Arthritis**
G. R. FEARNLEY, R. LACKNER, R. I. MEANOCK, and E. G. L. BYWATERS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 134–139, June, 1956. 6 figs., 3 refs.

In a pilot study of the value of a controlled " cross-over " trial at the Postgraduate Medical School of London 10 patients with generalized rheumatoid arthritis, whose main disability was severe involvement of one knee-joint, were divided into two equal groups. The first group received a total of four fortnightly injections of 2 ml. (100 mg.) of hydrocortisone acetate solution into the knee, followed after 8 weeks' rest by a total of four fortnightly injections of 4 ml. of 2% procaine solution into the same joint. They were then observed for a further 8 weeks. In the other group the same procedure was followed in the reverse order. Fortnightly assessments of progress were made on the basis of 9 criteria. No important changes occurred in respect of 4 of these, and 3 of the other 5 methods of assessment indicated greater improvement after the first course of treatment than after the second regardless of the drug used, the difference being statistically significant in each case. Assessment by reference to joint tenderness and limitation of extension indicated that, whichever drug was given first, hydrocortisone was slightly, but not significantly, more effective than procaine.

The authors consider that it would have improved the value of the test to have given a preliminary " training " course of treatment with some other therapeutic substance before starting the trial proper. They also stress the need for careful definition of the value of different criteria in assessment.

[It is noted that 2 ml. of hydrocortisone acetate solution is stated in the text to be equivalent to 100 mg. of the drug; the standard preparations, however, usually contain 25 mg. per ml.] *K. C. Robinson*

155. **Quantitation of the Activity of Rheumatoid Arthritis. 2. Recession of Morning Stiffness as Patients Go into Remission**
J. LANSBURY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 8–11, July, 1956. 3 figs., 1 ref.

This paper from Temple University School of Medicine, Philadelphia, reports an inquiry into the measurement of the duration of morning stiffness as a reliable sign of activity of the disease process in rheumatoid arthritis. Morning stiffness has long been recognized as an early

and almost universal clinical feature of this disease and the author presents data collected over a period of 10 years in 100 consecutive cases. It is shown that the duration of severe stiffness is correlated roughly with the erythrocyte sedimentation rate as measured by Cutler's technique (maximum 5-minute fall). On the other hand it appears to be unrelated to such features as age, sex, duration of the disease, and haemoglobin level. The author considers, therefore, that since most patients can note accurately the duration of morning stiffness, this should be recorded as a routine and will serve as an index of progress or the reverse. *W. S. C. Copeman*

156. **Quantitation of the Activity of Rheumatoid Arthritis. 3. The Maximum 5-minute Cutler Sedimentation Rate as an Index**

L. LANSBURY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 12–16, July, 1956. 3 figs., 1 ref.

For many years the erythrocyte sedimentation rate (E.S.R.) has been accepted as a rough guide to the degree of activity of the systemic disease in cases of rheumatoid arthritis. Unfortunately, its estimation may be carried out in a number of different ways, the results of which are not comparable with each other. The present author advocates Cutler's method, which differs from the others in common use in that a wide-bore tube is used and that the fall of the erythrocytes is measured not only at the end of an hour, but also at 5-minute intervals during that hour, the shape of the curve constructed from these readings being considered to provide additional information regarding the degree of activity present. As a measure of the slope of the curve, the maximum fall in any 5-minute period (the 5-minute E.S.R.) is recorded.

It is considered that the results of a statistical analysis of the findings in 10 cases of rheumatoid arthritis going into remission "indicates a trend toward normal, both for individuals and for the group, which is sufficiently regular to validate the Cutler 5-minute E.S.R. as a quantitative index of systemic rheumatoid activity". The author suggests that other methods, such as Westergren's, should be evaluated in a similar manner.

W. S. C. Copeman

157. **Rheumatoid Spondylitis and Aortic Insufficiency**

D. P. SCHILDER, W. P. HARVEY, and C. A. HUFNAGEL. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 11–17, July 5, 1956. 6 figs., 18 refs.

Rheumatoid spondylitis was discovered in 5 out of 100 cases of aortic insufficiency which were seen at Georgetown University School of Medicine, Washington, D.C., for surgical correction of the valve lesion. There was thus some selection of cases, both as regards the severity and the type of valve lesion, but the authors state that in several hundred cases of mitral stenosis similarly selected they have not observed one in which there was associated rheumatoid spondylitis.

The findings in these 5 cases were remarkably similar. All the patients were males (60 of the original 100 were males) and all showed possible disease activity, as evidenced by a raised erythrocyte sedimentation rate and anaemia. The spondylitis was severe, having lasted for an average of 23 years. None of the patients gave a history of syphilis; only one had had rheumatic fever and one peripheral rheumatoid arthritis (no residual manifestations). The known average duration of heart disease was 10 years; in the authors' view the clinical signs were those of gross aortic incompetence, although mitral diastolic murmurs were heard. Of the 5 patients, 3 died suddenly. At necropsy on 2 of these the mitral valves were normal and no Aschoff bodies were found; the aortic valves were thickened, shortened, and incompetent, but had no commissural irregularity or obliteration. In one case all layers of the aortic root were involved.

The authors state that a direct relationship must exist between rheumatoid spondylitis and heart disease, particularly that affecting the aortic valve.

J. Warwick Buckler

158. **The Effects on Ventilation of Thoracic Rigidity Secondary to Ankylosing Spondylitis.** (Les conséquences ventilatoires de la rigidité thoracique secondaire à la spondylarthrite ankylosante)

J. GIRARD, P. LOUYOT, P. SADOUL, and J. GRAIMPREY. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 2300–2310, July 2, 1956. 9 figs., 31 refs.

At the laboratories of the Faculty of Medicine, Nancy, tests of respiratory function were carried out on 61 patients with ankylosing spondylitis, of whom 44 were free from respiratory disease, but nevertheless showed diminished function. The mean value for total vital capacity in the patients was 3,120 ml., as against 4,463 ml. in 363 control subjects. The maximum volume of air expired during the first second after a forced inspiration was also diminished as compared with controls. The authors state that these changes are due to strictly mechanical factors consequent on costo-vertebral ankylosis, which combine to limit the functional respiratory potential under effort. The anatomical changes and their effect on respiration are irreversible and persist after the disease has ceased to be active.

G. W. Csonka

159. **Skin Changes in Ankylosing Spondylitis.** (Modifications tégumentaires de la spondylarthrite ankylosante)

P. FLORENTIN, P. LOUYOT, —. MACINOT, and B. PIERSON. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 2311–2315, July 2, 1956. 7 figs.

In an examination of nearly 100 patients [actual number not stated] with ankylosing spondylitis for changes in the skin it was found that 65% showed varying degrees of scleroderma-like abnormalities, especially in the lumbar area. Histological examination was carried out on biopsy specimens in 28 cases; of these, the skin was found to be normal in 4, but the others gave a positive MacManus reaction and showed deficient elastic fibres in the skin sections. In the more severe cases the abnormalities extended to the anterior aspect of the trunk. The high incidence of these skin changes suggests that in ankylosing spondylitis the connective tissue is profoundly affected. [No clinical details of the patients or of the type of preceding treatment are given.]

G. W. Csonka

Neurology and Neurosurgery

160. **Facial Paralysis and Muscle-relaxant Anesthesia**
P. M. OSMUN. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 529, May, 1956.

The case of a woman aged 32 who was operated on for chronic left mastoiditis with fistula of 10 years' duration under muscle-relaxant anaesthesia is described as a warning against the use of this type of anaesthesia in cases in which identification of the 7th cranial nerve is important for its preservation.

At operation the mastoid bone was found to be eburnated and only one mastoid cell was seen 1 mm. below the external canal and 1 mm. behind the crest of the facial ridge. This aroused some suspicion, but pressure with the back of a curette did not cause any facial twitch; this procedure was repeated four times during lowering of the bridge, each time without any response. At the end of the operation the patient immediately regained consciousness, but with a complete facial paralysis. It was then realized that she had been under nitrous-oxide–oxygen anaesthesia by intubation with a continuous drip of succinylcholine; the latter had been enough to cause complete muscular relaxation by blocking the myoneural junctions and had thus entirely abolished any response to stimulation of the facial nerve. Next day the cavity was explored, when it was found that the facial nerve, grossly swollen and injected, was uncovered for 1·5 cm. in the descending portion. A linear black streak was noted in the external semicircular canal, and pressure on the stapes forced bubbles out of the fistula. *F. W. Watkyn-Thomas*

161. **Use of Hexamethonium and Dibenzyline in Diagnosis and Treatment of Causalgia**
F. D. FOWLER and M. MOSER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 1051–1053, July 14, 1956. 6 refs.

In view of the fact that surgical interruption of the sympathetic pathways has been shown to be effective in the treatment of certain cases of causalgia, the authors have studied the effect on this condition of "dibenzyline" (N-phenoxy*iso*propyl-N-benzyl-β-chloroethylamine hydrochloride), which blocks the effect of adrenaline peripherally without affecting conduction through the ganglia, in conjunction with hexamethonium, which is a ganglion-blocking drug. At the Walter Reed Army Hospital, Washington, D.C., 25 patients were treated, all of whom had pain in an extremity with some of the features of causalgia, though in some cases the condition was not typical. The patient was first given an intravenous injection of 50 mg. of hexamethonium in 10 ml. of saline over 10 to 15 minutes, the injection being stopped if complete relief of pain was obtained before the full dose had been given. If the response was positive dibenzyline was given by mouth, starting with 10 mg. 4 times daily and increasing gradually until the maximum effect was obtained or a daily dosage of 120 mg. had been reached, the course of treatment lasting 3 weeks. Hypotensive side-effects were usually noted at dosages above 80 mg. daily.

Of the 25 patients, 6 needed no further treatment after one or two courses, and 13 others had complete relief while receiving this treatment, though pain recurred to some extent when it was stopped; 4 of these patients later underwent sympathectomy with permanent relief. Three patients obtained only partial relief and 3 showed no improvement, but in 3 of these 6 cases subsequent sympathectomy gave no better result.

The authors conclude that these drugs are of value not only for giving either permanent relief of causalgia or temporary alleviation until sympathectomy can be performed, but also for predicting the outcome of the operation. *J. W. Aldren Turner*

BRAIN AND MENINGES

162. **The Growth and Behaviour of Puppies with an Intact Cerebral Cortex after Extirpation of the Basal Ganglia (Caudate Nuclei).** (Развитие роста и поведения щенков с удаленными подкорковыми ядрами (хвостатыми телами) при сохраненной коре больших полушарий)
B. N. KLOSOVSKIĬ and N. S. VOLZHINA. *Архив Патологии* [*Arkh. Patol.*] **18**, 35–42, No. 1, 1956. 3 figs., 11 refs.

The caudate nuclei were extirpated in puppies on one or both sides and the animals then studied for periods varying up to 20 months. After a postoperative period marked by behaviour and motor disturbances, the animals recover and show no retardation of growth. They are capable of reproduction. Later behaviour varies in different animals. Some are mobile, excitable, and somewhat aggressive, being also easily frightened and inhibited. They run and jump well. Other dogs are more passive, frightened, and inhibited. Their movements are slow. Not all the dogs respond to their names, but they know the place of feeding and the kennels. *L. Crome*

163. **Paroxysmal Dysphasia and the Problem of Cerebral Dominance**
H. HÉCAEN and M. PIERCY. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 194–201, Aug., 1956. 12 refs.

The history of cerebral hemispheral dominance in relation to language and paroxysmal dysphasia is discussed. The authors then report the findings in 126 patients (97 right-handed and 29 left-handed) seen at the Hôpital Sainte-Anne, Paris, since 1947 who showed evidence of paroxysmal and unilateral cerebral dysfunction taking the form of Jacksonian attacks, various

pathological processes (confirmed at operation or necropsy), unilateral sensory or motor signs on examination, unequivocal lateralizing foci in the electroencephalogram, or unilateral lesions demonstrated by air encephalography or arteriography. Paroxysmal expressive dysphasia occurred significantly more frequently in left-handed patients with an aura than in right-handed patients with an aura, irrespective of the site of the epileptic focus. In right-handed patients the incidence of expressive dysphasia was much greater among those with left-sided disturbance than in those with right-sided disturbance, whereas no such difference was observed in left-handed patients. Paroxysmal receptive dysphasia was rare, except in right-handed patients with left-sided cerebral foci. Other tentative conclusions are drawn.

[It is impossible to summarize this paper briefly and those interested in this important subject are strongly advised to read the paper *in toto*.] *Hugh Garland*

164. **Tracheostomy, and Management of the Unconscious Patient**

J. ANDREW. *British Medical Journal* [*Brit. med. J.*] 2, 328–332, Aug. 11, 1956. 10 refs.

Tracheostomy has been employed as a means of maintaining a clear airway in an unconscious patient on 16 occasions in the past 4 years in the Department of Neurological Surgery at St. Bartholomew's Hospital, London, with incision of the trachea at the level of the second or third ring. The technique is described and various details discussed. It is emphasized that in cases of coma tracheostomy should be an elective procedure and its performance should not be delayed until the patient has become cyanosed or has developed peripheral circulatory failure.

The main indications for the procedure in the present series were: (1) coma persisting for more than 24 hours, when frequent suction was required to remove secretions from the pharynx and trachea; (2) difficulty in performing tracheal intubation (which, in any case, can give only temporary relief, since damage to the vocal cords may occur if an endotracheal tube passed through the larynx is left in position for more than 24 hours, while passage of a fine catheter down the tube for suction may be difficult); (3) the development of a lower respiratory infection in stuporous patients; and (4) shallow respiration—by halving the dead space, tracheostomy results in a relative increase in tidal volume.

R. G. Rushworth

165. **The Pathological Effects of Cerebral Arteriography**

T. CRAWFORD. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 217–221, Aug., 1956. 8 figs., 1 ref.

The author, from St. George's Hospital Medical School, London, reports a study of the pathological changes found at necropsy on 75 subjects on whom cerebral arteriography had been performed at intervals varying from 2 hours to 8 months before death, the material coming from many different sources. There was a surprisingly high incidence of complications, some being of a very sinister nature. Varying degrees of concealed haemorrhage from the site of arterial puncture were seen, sometimes of a gross order; this was usually minimal in young patients and most marked in elderly hypertensives, especially if the puncture had been repeated. Occasionally sterile abscess formation was related to the intramural injection of contrast medium. The most serious complication, because of its direct effects and because it is the precursor of embolism, was thrombosis. Mural thrombosis was a frequent finding: indeed, in a minor degree it was almost constantly present. In several instances there was evidence of cerebral embolism, and in a few cases traumatic false aneurysms or dissecting aneurysms were observed.

The incidence of these serious complications suggests that: (1) arteriography should be reserved for the study of gross disease; (2) it should be used with special caution in the elderly, arteriosclerotic, hypertensive subject; (3) puncture adjacent to the carotid bifurcation should be avoided; and (4) the vessel should not be punctured more than once and should never be transfixed.

Hugh Garland

166. **Subarachnoid Haemorrhage Due to Intracranial Aneurysms. Results of Treatment of 249 Verified Cases**

W. MCKISSOCK and L. WALSH. *British Medical Journal* [*Brit. med. J.*] **2**, 559–565, Sept. 8, 1956. 1 fig., 9 refs.

The mortality from subarachnoid haemorrhage due to ruptured aneurysm during the 8-week period following admission of the patient to hospital has been stated to be 50%. With this in mind, the authors of this paper from St. George's Hospital, London, report a study of the results of surgery in 249 cases of proved intracranial aneurysm associated with subarachnoid haemorrhage, comparing these with the results of conservative treatment. It is pointed out that little information of real value can be obtained from series of cases of subarachnoid haemorrhage in which the situation and nature of the lesion have not been established. It is essential for certain factors to be evaluated if the results of differing forms of treatment are to be compared.

Comparative figures for the results of surgical and medical treatment as seen in relation to the severity of the effects of haemorrhage, the age of the patient, and the presence or absence of hypertension are given in a number of tables. The value of different forms of treatment in relation to the actual site of the aneurysm is discussed, as is the incidence of associated intracerebral, intraventricular, and subdural haemorrhage, and recurrent haemorrhages. The authors consider their figures to indicate that with early investigation and treatment of cases of bleeding aneurysm the mortality is lower than that to be expected from the natural course of the disease. They are convinced that, "compared with purely conservative measures", surgery results in "a definite lowering of the mortality rate".

[This paper emphasizes the need for consideration of different types of aneurysm instead of unrealistically grouping all intracranial aneurysms together. It should be read by all who have to treat cases of subarachnoid haemorrhage.] *J. V. Crawford*

167. **Intrasellar Aneurysms.** (Intraselläre Aneurysmen) W. SCHIEFER and F. MARGUTH. *Acta neurochirurgica* [*Acta neurochir.* (*Wien*)] **4**, 344–354, 1956. 3 figs., bibliography.

This paper from the University of Cologne describes the clinical picture, differential diagnosis, and treatment of intrasellar aneurysms, which arise extradurally from the infraclinoid part of the internal carotid artery near the point of origin of the ophthalmic artery. In a series of 72 cases of saccular aneurysm the authors found 3 which were intrasellar and a further case was referred to them. The main signs and symptoms in these 4 cases were: (1) onset with severe headache, often unilateral; (2) early dimming of vision leading to unilateral loss of vision; (3) absence of signs of raised intracranial pressure; (4) little or no endocrine disturbance; and (5) *x*-ray evidence of calcification in the region of the sella turcica, which was either enlarged or normal in size. Such aneurysms may be demonstrable by angiography, but a negative result is not uncommon owing to thrombosis in the aneurysmal sac. The differential diagnosis from hypophyseal tumour, suprasellar meningioma, craniopharyngeoma, nasopharyngeal tumour, metastases, and basal arachnoiditis is discussed. In general, treatment consists in ligation of the affected internal carotid artery in the neck after the demonstration of an adequate collateral circulation. *J. B. Stanton*

168. **Carotid Artery Occlusion**
J. E. WEBSTER, E. S. GURDJIAN, and F. A. MARTIN. *Neurology* [*Neurology*] **6**, 491–502, July, 1956. 13 figs., 20 refs.

Angiography was carried out on 70 patients (54 males and 16 females) suffering from major "stroke" syndromes or recurrent "strokes" at the Grace and Memorial Hospitals, Detroit. Thrombosis of the internal carotid artery was found in 64, of the carotid bifurcation in 5, and of the common carotid artery in one case. The left side was involved in 37 instances. The clinical findings included hemiparesis or hemiplegia in 57 cases, aphasia in 25, headache in 15, abnormal mental states in 13, hemihypoalgesia or hemiparaesthesiae in 12, coma in 10, seizures in 6, optic atrophy in 4, homonymous field defect in 3, and vascular disease elsewhere in the body in 8. Blood pressure was normal in 57 cases. Electroencephalograms, which were obtained in 38 cases, showed focal abnormalities in 32 and generalized abnormalities in 3.

In 41 of the cases exploration of the neck and excision of a portion of the thrombosed vessel near the bifurcation were carried out. The thrombosed internal carotid artery was seen to be swollen or collapsed. In many cases the external carotid artery had undergone compensatory dilatation. Microscopical examination showed atherosclerosis in all cases. Where complete organization of fibrin clots had taken place near the bifurcation vessels were seen, indicating an attempt at canalization. Distortions in the bulb area suggested plaques, stenosis, and narrowing of the vessel; the authors point out that these abnormalities may result in a reduction in the blood flow with consequent ischaemia of the brain and cerebrovascular accidents of varying intensity and duration. In 3 cases reconstruction of the bifurcation was carried out after excision of the atheromatous segment; in each case there was re-thrombosis of the vessel. In several instances excision of the totally occluded internal carotid artery was followed by cessation of repeated cerebrovascular attacks.

It is suggested that the occasional dramatic effect of stellate block or infiltration of procaine around the artery may be due to relaxation of a thrombosing vessel undergoing spasm. *G. de M. Rudolf*

169. **Spontaneous Occlusion of the Middle Cerebral Artery**
E. H. FEIRING and B. J. SUSSMAN. *Neurology* [*Neurology*] **6**, 529–546, Aug., 1956. 24 figs., 23 refs.

170. **Acute Hemorrhagic Encephalitis**
K. KRISTIANSEN, W. HARKMARK, and M. M. COHEN. *Neurology* [*Neurology*] **6**, 503–509, July, 1956. 6 figs., 33 refs.

Betweeen December, 1953, and June, 1954, 5 cases of acute haemorrhagic encephalitis were seen at Ullevål Hospital, Oslo. The ages of the patients, 3 males and 2 females, ranged from 31 to 51 years. Headache, fever, and cough preceded symptoms of nervous-system involvement, which included hemiparesis, stupor, hemihypoaesthesia, quadriplegia, central facial palsy, papilloedema, neck rigidity, confusion, disorientation, hallucinations, diplopia, and dysphasia, the most common being hemiparesis and stupor. In all cases there was leucocytosis and the erythrocyte sedimentation rate was high. The cerebrospinal-fluid cell count was normal in 3 cases, a pleocytosis being present in 2. The angiographic appearances suggested the presence of a space-occupying lesion, but in 3 cases they were due to prominent displacement of the anterior cerebral artery by oedema. The electroencephalogram in 2 cases showed continuous delta activity or abnormal potentials. Craniotomy was performed in all cases. Examination of a biopsy specimen of cerebral parenchyma in 4 cases revealed demyelination, diffuse scattering of polymorphonuclear leucocytes, and varying numbers of mononuclear cells. Areas of haemorrhage, unrelated to the operation, were found in 3 cases.

Of the 5 patients, 3 died in the acute phase of the disease. One of the survivors had an incomplete left-sided hemianopia only, in spite of the initial stupor, hemiparesis, diplopia, and disorientation; the other survivor, however, still showed signs of mental deterioration, disorientation, and confusion. At necropsy congestion of the meningeal vessels, with scattered areas of subarachnoid haemorrhage and parenchymal oedema, was found. Herniation of the cingulate gyrus across the midline was noted in 2 cases. Microscopical examination revealed hyperaemia of the meningeal vessels, blood in the subarachnoid space, and inflammatory cells in the meningeal tissue. In acute cases the cells were chiefly polymorphonuclear leucocytes, and in the more chronic cases the meningeal infiltrate consisted of plasma cells. Demyelination in the centrum ovale and in the

deeper parts of the white matter, chromatolysis and swelling of many cortical neurones, endothelial proliferation, and congestion of the parenchymal vessels were also noted.

This series of cases demonstrates that haemorrhagic encephalitis is not invariably fatal, although the diagnosis can usually be made only at operation or at biopsy. The differential diagnosis is from a space-occupying lesion or a cerebrovascular accident. There is little correlation between symptoms and the pathology. In the authors' view, the occurrence of 5 cases in 7 months, although none was seen during the preceding 2-year period, suggests the possibility of a toxic or infectious aetiology. *G. de M. Rudolf*

171. **Anticonvulsant Action of Diamox in Children**
J. G. MILLICHAP. *Neurology* [*Neurology*] **6**, 552–559, Aug., 1956. 3 figs., 11 refs.

In recent experiments on animals the author and others have shown (*J. Pharmacol.*, 1955, **115**, 251) that the anticonvulsant action of acetazolamide (" diamox ") is independent of the acidosis produced, being in fact directly related to the inhibition of carbonic anhydrase in the brain. To obtain clinical support for these laboratory findings the effect of acetazolamide on " seizures of the type not specifically responsive to acid–base changes " was studied in 14 children aged 6 months to 11 years at the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland. In all cases the seizures were of organic aetiology, being secondary to a traumatic lesion or developmental disorder of the brain. Grand mal occurred in 13 cases, and in 5 of these was associated with generalized myoclonic jerks. In one case myoclonic attacks occurred alone. The addition of acetazolamide to the previous therapeutic regimen (which was continued throughout the trial period of 5 to 26 weeks) reduced the frequency of the seizures in every case—in 8 cases by over 75%. Major seizures were better controlled than those of the myoclonic type. In addition, in 5 children the effect of acetazolamide, given alone, on the incidence of major and myoclonic seizures was compared with that of " dilantin " (phenytoin), the response to the two drugs being found to be almost identical.

The average anticonvulsant dose of acetazolamide was 28 (range 18 to 36) mg. per kg. body weight daily, but 8 patients developed tolerance to the drug and in 7 of these cases acetazolamide treatment was discontinued after completion of the trial. Toxic effects occurred in 10 cases, and included anorexia and polyuria in 5 cases each, nocturnal enuresis in 4, drowsiness in 3, and vomiting and diarrhoea in one each. These side-effects were relatively mild and, with the exception of anorexia and lassitude, did not persist.

The author concludes that these clinical findings are compatible with the laboratory findings and suggests that " further investigation of the anticonvulsant action of carbonic anhydrase inhibitors may elucidate the seizure mechanism ". [However, it would appear that the clinical value of acetazolamide is definitely limited by the development of tolerance in more than half the cases treated.] *A. G. Freeman*

NEUROMUSCULAR DISORDERS

172. **Progressive Fluctuating Muscular Rigidity and Spasm (" Stiff-man " Syndrome): Report of a Case and Some Observations in 13 Other Cases**
F. P. MOERSCH and H. W. WOLTMAN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **31**, 421–427, July 25, 1956.

The authors describe a syndrome which they first saw in 1924 in a man aged 49 who was admitted to the Mayo Clinic suffering from a progressive disorder characterized by stiffness and rigidity of muscles, beginning in the muscles of the neck and gradually spreading to involve those of the shoulders and upper limbs, trunk, abdomen, and thighs. The rigidity was punctuated by intermittent painful spasms which could be precipitated by noise or sudden movement and were sometimes severe enough to throw the patient to the ground. As rigidity increased kyphosis developed, the patient's gait became slow and awkward, and all movements were slowly performed. Apart from the muscular rigidity, which on examination showed some fluctuation, there were no other neurological signs. Over the subsequent 30-year period the authors have observed 13 similar cases, the average age of the patients (9 males and 4 females) at onset being 41·5 years. Follow-up, which was possible in 11 of the 14 cases, showed that 7 of the patients were alive, and in all but one the muscular rigidity had increased steadily over periods of 2 to 15 years. In all cases the clinical picture was similar to that described above—muscular rigidity and painful spasms, with secondary spinal deformity and slowness and poverty of movement, being the predominant features. On examination widespread " boardlike " rigidity of the muscles was evident and usually the deep tendon reflexes were brisk. In 4 cases reducing substances were present in the urine but the blood sugar level was normal. The results of other laboratory investigations, which included determination of the blood count and electrolyte balance and examination of the cerebrospinal fluid, were normal. Electromyographic examination of rigid muscles in 5 cases gave a pattern of normal volitional activity, while muscle biopsy in 2 revealed no abnormality. Treatment with sedatives, cortisone, and various antispasmodics was of no value.

The authors admit that there is nothing in the findings which would indicate the nature of this disorder. They note its similarity to chronic tetanus, but give reasons for excluding this diagnosis; they suggest that it may be due to a specific metabolic disorder. [It seems possible that the condition may be an atypical form of torsion spasm (dystonia musculorum deformans).] *John N. Walton*

173. **Benign Congenital Myopathy with Myasthenic Features**
J. N. WALTON, N. GESCHWIND, and J. A. SIMPSON. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 224–231, Aug., 1956. 2 figs., 16 refs.

Psychiatry

174. **The Electroencephalogram in Dementia. Some Preliminary Observations and Correlations**
H. WEINER and D. B. SCHUSTER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 479–488, Aug., 1956. Bibliography.

The authors have studied the electroencephalogram (EEG) in 71 cases of organic dementia. Care was taken to exclude cases of delirium and those patients with neurological signs in whom there might be focal cerebral lesions likely to affect the EEG. The cases were divided into three clinical groups: (1) minimal dementia (minor disturbances of attention span and abstract thinking), (2) moderate dementia (additional defects of recent memory, retention, and recall), and (3) severe dementia (impairment of remote memory and orientation and other signs of disorganization of thought). At least 2 recordings of the EEG were taken in each case.

In only 16 cases (22%) was the EEG normal; in 52 of the remaining 55 the abnormality took the form of diffuse slow (theta or delta) activity, while in the other 3 cases excessive fast activity was present. There was a statistically significant relationship between the degree or dementia, regardless of its aetiology, and the degree of abnormality in the EEG. The record was no more often abnormal in patients who showed major disturbance of mood, thought content, and behaviour than in those with uncomplicated sensorial defect. None of the individuals with normal records had a severe degree of dementia. *John N. Walton*

175. **Prefrontal Leucotomy. Views of Patients and Their Relatives**
A. ELITHORN and E. SLATER. *British Medical Journal* [*Brit. med. J.*] **2**, 739–742, Sept. 29, 1956. 9 refs.

In view of the current divergence of opinion on the value of prefrontal leucotomy in the treatment of mental disorders, the authors have analysed the results in all patients who had undergone leucotomy for a variety of conditions at the National Hospital for Nervous Diseases, Queen Square, London, up to June, 1954, the assessment of the effect of the operation being made in each case entirely by the patient and his relatives. The survey included 103 of the 118 patients treated, 5 of the remaining 15 having died as a result of the operation and the information required about the others not being available for various reasons. The patient was asked 6 questions: (1) whether the operation had helped him and, if so, how; (2) which symptoms, if any, had improved; (3) which symptoms had not improved; (4) what bad effects, if any, had resulted from the operation; (5) whether he had noticed any change in personality; and (6) whether he was glad or regretted that he had undergone the operation. In addition to questions corresponding to the first 4 above, the relative was asked: to assess the value of the operation to the patient on a 5-point scale ranging from " much improved " to " much worse "; whether, with his present knowledge, he would in similar circumstances again give his consent to the operation; and how the operation had affected his own relationship with the patient. (A relative's views were obtained in 93 cases (90%).)

The analysis is concerned with answers to the general questions only, those dealing with particular symptoms being omitted. In the majority of cases patient and relative agreed as to the effect of treatment; 65% of the patients were glad they had had the operation, and the relative thought that there had been an improvement in 78% of cases. In only 2 cases in which the patient was glad did the relative consider the patient to be worse, while of the 72 cases in which the relative reported improvement, only in 5 was the patient sorry he had had the operation. A distinction is made between personality changes and bad effects, as in some cases beneficial personality changes were claimed. The patient denied both bad effect and personality change in 46 cases; 14 patients reported no bad effect and helpful personality change; 11 reported unpleasant personality change without other bad effect; and 32 reported bad effects from the operation, with unwelcome personality change in 15 cases. Very much the same picture was given by the relatives, with a slightly increased incidence of bad effects, which included irritability, laziness, tactlessness, emotional flatness, and memory defects.

The authors point out that assessment of the value of leucotomy must be subjective, whoever makes it, and that assessment from the patient's viewpoint often takes second place to that of the physician, but is equally necessary. *E. H. Johnson*

176. **Five-year Follow-up of Patients Subjected to Three Different Lobotomy Procedures**
N. L. PAUL, E. FITZGERALD, and M. GREENBLATT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 815–819, June 30, 1956. 1 fig., 10 refs.

The long-term results of frontal lobotomy in 116 mentally ill patients are discussed in this paper from Harvard Medical School and the Psychopathic Hospital, Boston. Of the 116 patients, 91 had schizophrenia; 56 had been ill for more than 10 years and only 19 for less than 5 years. All the patients had failed to respond to insulin coma treatment, electric convulsion therapy, and intensive psychotherapy. The patients were divided at random into three groups, on which three different types of operation were performed—that is, bilateral frontal leucotomy, unilateral frontal leucotomy, or bimedial lobotomy in which the division of fibres was restricted to the medial side of the frontal lobes. In the 5-year follow-up assessment particular attention was paid to intellectual function, tension, thought content, social adaptation, and work adjust-

ment. In general, the results in patients who had undergone bimedial lobotomy were better than those in patients subjected to bilateral or unilateral leucotomy. Thus of 35 on whom bimedial lobotomy was performed, 12 were markedly improved at the end of 5 years, compared with 7 out of 39 subjected to bilateral and 6 out of 42 subjected to unilateral leucotomy. Of 116 patients, 24 reported the occurrence of seizures, but there was no significant difference between the three groups in the incidence of these seizures. *J. B. Stanton*

177. **Thorazine and Serpasil Treatment of Private Neuropsychiatric Patients**
F. J. Ayd. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 16–21, July, 1956. 1 fig., 1 ref.

The author describes the results observed in 300 private psychiatric patients of whom 150 were treated with chlorpromazine and 150 with reserpine, in varied dosage. Two-thirds of the patients were psychoneurotic and the remainder psychotic; the age range was from 14 to 82. Patients and relatives were warned of the probable side-effects of the drugs; most of these occurred, but were rarely serious and usually disappeared on reduction of the dosage. The results, which are categorized only as "improved" or "unimproved", were respectively as follows: in the chlorpromazine group 99 and 51, and in the reserpine group 84 and 66.

The effects of these drugs are regarded as calmative, non-specific, and most pronounced in those patients with central sympathetic excitability, as shown by reactions to the Funkenstein test. In the treatment of neurotic patients the author recommends chlorpromazine for those whose anxiety is associated with altered gastrointestinal function, and reserpine for those "whose anxiety is centred on the cardiovascular system". The danger that these drugs tend to increase already existing depression is pointed out. *A. C. Tait*

178. **Treatment of Hyperkinetic Emotionally Disturbed Children with Prolonged Administration of Chlorpromazine**
H. Freed and C. A. Peifer. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 22–26, July, 1956. 20 refs.

At Philadelphia General Hospital 25 children (20 boys and 5 girls) aged 7 to 13 were treated for periods of 4 to 16 months with empirically determined doses of chlorpromazine which ranged from 10 to 250 mg. daily; there was no marked toxicity. All the patients were over-active, disturbed, and many were combative; diagnostically, the majority were cases of primary behaviour disorder. Marked improvement occurred in 18 cases, and some improvement in 3, as assessed by the patients' behaviour and achievement at school, behaviour in the home, and by the changed responses on repetition of a battery of tests. Lessening of overactivity was outstanding. Psychologically, better intellectual functioning, facilitation of learning, and closer interpersonal relationships were observed. It is concluded that the damping of the "fight–flight response" in this manner should benefit the carrying out of complementary psychotherapy. *A. C. Tait*

179. **Response of Psychiatric Patients to Massive Doses of Thorazine [Chlorpromazine]: I. Behavioral and Clinical Analysis**
L. Rockmore, L. Shatin, and I. C. Funk. *Psychiatric Quarterly* [*Psychiat. Quart.*] **30**, 189–203, April, 1956 [received Aug., 1956]. 8 refs.

At the Veterans Administration Hospital, Albany, New York, an attempt was made to evaluate the effect of massive doses of chlorpromazine hydrochloride ("thorazine") on the psychiatric state (and particularly the behaviour) of 56 male in-patients who had proved refractory to other methods of treatment, but were otherwise unselected. There were 41 cases of schizophrenia, the remaining 15 having a variety of diagnoses. The drug was given by mouth, the daily dose increasing gradually from 150 mg. on the 1st day to 800 mg. on the 8th day, at which level it was maintained until the 13th day, after which it was reduced by half each day until it reached 50 mg. on the 17th day, this dose being then continued for a further 3 weeks. During the first 3 days the patient was confined to bed and hourly records made of the blood pressure, temperature, pulse, and respiration rate. Behaviour was assessed by the nursing staff on a 100-item "behavioral rating scale" before treatment, on the 11th day of treatment, and 3 weeks after treatment had been discontinued. (The three ratings were not necessarily made by the same nurse.) A clinical assessment was made after treatment according to a 5-step scale, slight and marked degrees of improvement and deterioration being distinguished, as well as "no change". (All the clinical ratings were made by the same psychiatrist.)

The mean behavioural and clinical ratings for the group as a whole showed that massive chlorpromazine therapy generally resulted in improvement, particularly in the fields of communication and socialization. The authors state that this improvement was most marked in the passive, non-communicative patient, and not necessarily in the hyperactive patient, whereas previous reports have stressed the value of chlorpromazine in cases in which excitement and the affective component predominate. They emphasize, however, that in view of the fact that their investigation lacked a control group the findings must be regarded as suggestive rather than definitive.
John A. Clark

180. **Insulin and Chlorpromazine in Schizophrenia. A Comparative Study in Previously Untreated Cases**
R. H. Boardman, J. Lomas, and M. Markowe. *Lancet* [*Lancet*] **2**, 487–491, Sept. 8, 1956. Bibliography.

In a comparative study carried out at Springfield Hospital, London, two comparable groups each consisting of 25 male and 25 female schizophrenic patients who had not received previous treatment were given either insulin coma therapy (up to 50 comas being induced, with additional electric convulsion therapy if required) or chlorpromazine (300 mg. daily for 3 months). There was no statistically significant difference between the short-term results of these two forms of therapy, although the authors are inclined to regard chlorpromazine as slightly more beneficial. *F. K. Taylor*

Dermatology

DERMATOSES

181. **Gastroscopic Studies in Rosacea**
B. USHER and G. YOUNG. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **75**, 111–113, July 15, 1956. 5 refs.

The authors of this paper from Montreal General Hospital consider that rosacea is part of a general vascular disturbance with the presenting signs on the face. Holding the view that the vessels of the gastric mucosa are also affected they carried out gastroscopy on 19 patients with rosacea; in 18 of these there were definite signs of superficial, atrophic, or hypertrophic gastritis. These changes were noted in only 4 out of 15 controls. All the patients were given the same treatment—local application of lotio alba, hydrochloric acid by mouth, and a bland diet—alcohol, coffee, tea, spices, and fried foods being forbidden [but the results are not stated]. In 4 cases gastroscopy was carried out while the rosacea was active and also while it was in remission; a normal gastric mucosa was consistently found during remission of the skin disease. *S. T. Anning*

182. **Liver Function in Cases of Pemphigus.** (Функциональное состояние печени у больных пузырчаткой)
H. V. KOLOKOLOVA. *Вестник Венерологии и Дерматологии* [*Vestn. Vener. Derm.*] 13–15, No. 3, May–June, 1956.

In a study of liver function carried out at the Second Medical Institute, Moscow, on 4 patients with dermatitis herpetiformis and 18 with pemphigus (12 cases of pemphigus vulgaris, 4 of pemphigus foliaceus, and 2 of pemphigus vegetans) enlargement and tenderness of the liver on palpation were found in 13 patients, and functional disturbances of the liver, which were slight at the beginning or in remission and more severe at the height of the disease, were present in the majority of cases. The excretion of hippuric acid was 2·6 to 1·8 g. in the early stages, but fell to 2·1 to 1·5 g. at the peak of the disease and still further, to 1 to 0·85 g., in fatal cases.

The serum cholesterol ester level was normal in all cases of dermatitis herpetiformis and in 3 of the cases of pemphigus, but in 15 cases of the latter condition it fell to between 50 and 38 mg. per 100 ml. and in severe cases to between 31 and 13 mg. per 100 ml.

The prothrombin index, which was normal at the onset, decreased to 70 to 80% of normal with deterioration of the skin and general condition; in 5 cases, shortly before death, it fell to 47 to 38% of normal. Increased urobilinuria was present in 11 out of 22 cases, but in the majority was transient, increasing with exacerbation of the disease and disappearing during remissions. In 2 cases there was no apparent relationship between urobilirubin excretion and the course of the disease. The serum bilirubin level in most cases was within normal limits. No abnormality in the glycogenic function of the liver was established.

[The laboratory methods employed in this study are not described.] *H. Makowska*

183. **A Comparison of Chloroquine and Gold in the Treatment of Lupus Erythematosus**
J. T. CRISSEY and P. F. MURRAY. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **74**, 69–72, July, 1956. 3 figs., 6 refs.

Results in the treatment with chloroquine of 24 cases of chronic discoid lupus erythematosus were compared to a standard derived from treatment of 66 cases with gold sodium thiosulfate. There was no significant difference in the proportion of cases that responded to these drugs. Cases treated with chloroquine responded more rapidly than those treated with gold. There was a significantly greater number of recurrences within a year after chloroquine treatment than after gold. No detectable correlation was observed between the duration of the disease before and the duration after treatment with either gold or chloroquine, or, in chloroquine-treated cases, between the age of the patient and the duration of the disease. There was a small amount of negative correlation between the patients' ages and the duration after treatment in cases treated with gold.

Serious side-effects following chloroquine therapy were not seen. Visual disturbances and incubus were observed. Chloroquine is superior to gold esthetically and in ease of administration.—[From the authors' summary.]

184. **The Treatment of Chronic Lupus Erythematosus with Resochin.** (Beitrag zur Resochinbehandlung des chronischen Lupus erythematodes)
E. THIEL. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **133**, 660–667, June 30, 1956. 12 figs., 9 refs.

The author, at the Charité Hospital, Berlin, has treated 101 patients with chronic lupus erythematosus with "resochin", an acridine derivative. Compared with "atebrin" (mepacrine) resochin does not produce any skin discoloration and acts more quickly, but relapse after discontinuation of treatment occurs with both drugs.

The dosage of resochin was 375 to 500 mg. daily by mouth for 7 to 10 days, later reduced to 250 mg. daily and finally to 125 mg. and maintained at that level until improvement or a total of 20 g. had been given. In case of relapse a second course proved effective. Local treatment was also given in addition (or alone in some cases) and consisted in the injection of up to 2 ml. of 10% resochin with 2% "jenacain–adrenaline" in the proportion of 2 to 1 into each lesion to a total of 5 ml. per patient, this being repeated at 8-day intervals. The injection produced a violent burning sensation.

Of the 85 female and 15 male patients, 79 were asymptomatic at the end of treatment and 7 did not respond at all. Some of the cured cases had previously failed to respond to mepacrine. The side-effects due to resochin, which were fewer and less severe than with mepacrine, included headache, vertigo, mild gastro-intestinal upsets, and loss of weight in some cases. In 10 cases intolerant of mepacrine resochin produced no side-effects.

F. Hillman

185. **Discoid Lupus Erythematosus Treated with Plaquenil**

T. CORNBLEET. *A.M.A. Archives of Dermatology [A.M.A. Arch. Derm.]* **73**, 572–575, June, 1956. 2 figs., 2 refs.

"Plaquenil" (7-chloro-4-[4-(N-ethyl-N-β-hydroxyethylamino)-1-methylbutylamino]-quinoline), a quinacrine type of drug, was given to 7 patients suffering from chronic lupus erythematosus which had responded only partially to other forms of treatment, and in this paper from the University of Illinois College of Medicine and Cook County Hospital, Chicago, the results are described. Each patient received an initial dosage of three 200-mg. tablets daily. Only one patient experienced any side-effect—namely, an attack of vomiting—and treatment was resumed satisfactorily on a smaller dosage after a fortnight's rest. Some involution of the lesions was observed in all cases, and the dosage was reduced to two tablets daily at 2 to 3 weeks. In 2 cases there was complete involution and in the remainder at least 40% involution. No changes were observed in the blood or urine as a result of this treatment. There was no skin staining. Preliminary experience suggests that plaquenil is less toxic than other antimalarial drugs of this type.

E. H. Johnson

186. **Plaquenil in the Treatment of Discoid Lupus Erythematosus. A Preliminary Report**

H. M. LEWIS and G. M. FRUMESS. *A.M.A. Archives of Dermatology [A.M.A. Arch. Derm.]* **73**, 576–581, June, 1956. 2 figs., 13 refs.

A clinical study is reported of the effect of "plaquenil" [see Abstract 185] in the treatment of 22 patients with discoid lupus erythematosus, of whom 6 had not been treated before, 11 had not responded satisfactorily to previous treatment, and 5 had been unable to tolerate other medication because of severe side-effects. The dosage initially was two 200-mg. tablets 4 times a day. If this dose was well tolerated and there were signs of improvement the dosage was reduced slowly, usually by 200 mg. every few days. Over a trial period of 4 months 17 patients showed more than 50% improvement while 9 became free from all signs of disease activity. Side-effects—notably diarrhoea, intestinal cramps, nausea, and dizziness—necessitated cessation of treatment in 15 cases; after a rest period treatment was resumed with a smaller dosage, which was usually tolerated.

The authors conclude that plaquenil offers considerable promise in the treatment of discoid lupus erythematosus, but that further study, particularly of the effective dosage, is required.

E. H. Johnson

DERMATITIS

187. **Nickel Dermatitis**

C. D. CALNAN. *British Journal of Dermatology [Brit. J. Derm.]* **68**, 229–236, July–Aug., 1956. 2 figs., 7 refs.

An analysis is presented of 400 cases (all in women) of contact dermatitis due to nickel, which, the author states, is by far the commonest sensitizing agent now encountered in routine dermatological practice in London.

In 381 of the 400 cases the first manifestation was stocking-suspender dermatitis; in the remaining 19 the dermatitis began under ear-rings (13), wrist watch (3), brassière clips (1), necklace clasp (1), and spectacle frame (1). The dermatitis occurs as a primary eruption at sites of direct contact, and as a secondary eruption, which behaves like a haematogenous spread similar to the -id phenomenon in ringworm and is usually symmetrical. The secondary sites are elbow flexures, eyelids, sides of the neck and face, and the inner side of the thighs. Secondary spread is more frequent in suspender dermatitis (75% of cases) than in any other type of eczema; it occurs next most commonly in varicose eczema (34%).

Nickel sensitivity can be confirmed by patch-testing with 1% or 2·5% nickel sulphate solution. Cross sensitivity with other metals—for example, cobalt and copper—may occur, and multiple contact sensitivity is not uncommon. The author considers that the allergy to nickel is almost certainly permanent, since in none of these cases was there a change on patch-testing from positive to negative. Friction, sweating, and emotional disturbances are probably contributory aetiological factors, but are difficult to assess. Chronic eczema of the elbow flexures in women with a background of emotional stress may readily be diagnosed as neurodermatitis, but in fact many of these patients are sensitive to nickel.

The prognosis is very variable. When secondary spread has occurred the dermatitis may take a long time to clear up and in a high proportion of cases there are recurrences. Suspender dermatitis appears to predispose to eczema elsewhere, especially on the hands.

E. W. Prosser Thomas

188. **Effects of Nickel on the Skin**

G. C. WELLS. *British Journal of Dermatology [Brit. J. Derm.]* **68**, 237–242, July–Aug., 1956. 2 figs., 10 refs.

In an investigation of the effects of nickel on the skin it was shown that the horny layer has an affinity for the metal, which is taken up by certain keratins from great dilution. This is also true of the inner root sheath of hairs, but not of the cortex of hairs above the growth zone or of mucosa. Chemical tests suggest that the carboxyl groups of keratin may play a part in retaining nickel. Under conditions of patch-testing nickel tends to accumulate in surface scales, but may penetrate more deeply at sweat-duct and hair-follicle ostia, or at areas of surface damage. Because of the high incidence of eczema of the hand in women who had become sensitized to nickel from stocking suspenders, it has been suggested

that small amounts of nickel in detergents might be sufficient to elicit nickel dermatitis of the hands. Spectrographic analysis, however, of samples of 6 detergent powders commonly used in Britain revealed no nickel down to the limit of sensitivity for the analytical method.

The author states that in his experience it is rare for nickel sensitivity to be induced by anything other than the stocking suspender. He suggests the use of suspender buckles made from nylon, since other materials are not wholly satisfactory and it is known that pure nylon never sensitizes. *E. W. Prosser Thomas*

[These papers appear to cover much the same ground as the paper by the same authors in the *British Medical Journal* of June 2, 1956, p. 1265 (*Abstracts of World Medicine*, 1956, **20**, 395)—EDITOR.]

189. **Clinical and Histological Changes in the Peripheral Lymph Nodes in Cases of Tuberculosis Cutis.** (Клинико-цитологическая характеристика периферических лимфатических узлов у больных туберкулезом кожи) O. V. LITOVCHENKO. *Вестник Венерологии и Дерматологии* [*Vestn. Vener. Derm.*] 8–12, No. 3, May–June, 1956. 2 figs., 16 refs.

The clinical and histological changes in the peripheral lymph nodes were studied in 439 patients at the Institute of Cutaneous Tuberculosis, Moscow, the series including 265 cases of lupus vulgaris, 69 of tuberculosis colliquativa, 90 of tuberculide, 11 of tuberculosis verrucosa, and 4 of Boeck's sarcoid. The lymph nodes were enlarged in 97% of cases of lupus vulgaris and tuberculide, and in all the cases of the other conditions. A brief description of the consistency and distribution of the enlarged nodes is given, and it is pointed out that in lupus vulgaris suppuration or even softening of the nodes was never encountered, although it was a frequent finding in cases of the colliquative and disseminated forms of tuberculosis cutis.

Microscopical examination of lymph-node biopsy material was made in 247 cases. A typical finding was lymphadenoid hyperplasia showing cells in different stages of development, and in many cases groups of epithelioid cells and caseous masses were found. The author concludes that the clinical appearance and histological picture of the lymph nodes are sufficiently distinctive to afford additional help in the differential diagnosis of tuberculosis of the skin. *H. Makowska*

190. **The Swimming Pool Disease (Mycobacteriosis Balnearea).** [In English]
L. ZETTERGREN and B. ZETTERBERG. *Acta Societatis medicorum Upsaliensis* [*Acta Soc. Med. upsalien.*] **61**, 47–74, June 30, 1956. 23 figs., 17 refs.

The literature on " swimming-pool disease ", a specific condition in which granulomatous lesions appear on the skin after an abrasion received in a public swimming pool, is reviweed, and a detailed study of 72 cases, with special reference to the infecting organism, is presented in this paper from the Universities of Gothenburg and Uppsala.

The sex incidence was equal, and the ages of the patients ranged from 5 to 20 years, 66 being between 11 and 14 years of age. Most of the patients remembered that the lesions appeared directly after a scratch sustained in a swimming pool, but one patient insisted that he had never used a public swimming pool. A single bony prominence, usually the elbow, was affected in 2 cases, but in 4 there were several foci and in 2 cases lesions recurred on another site some months after the initial attack. The skin lesion was a pustule which at first was the size of a rice grain, growing to the size of a pea in a few weeks; during this time the pustule ulcerated, having a shallow crater and being capped with a brown–black crust. The regional lymph nodes were occasionally affected, but no constitutional disturbance was noted. The lesion healed with a soft, shiny scar.

Histologically, the skin lesions showed a diffuse epithelioid-cell reaction with tubercle formation and, occasionally, caseous necrosis; microscopically, the changes in the lymph nodes could not be differentiated from those of tuberculosis. Detailed bacteriological investigations, which included animal inoculation, were carried out to determine the nature of the acid-fast, Gram-positive, rod-shaped organism present in the tissue and in the swimming pool. Morphologically, this was indistinguishable from Koch's bacillus, but the cultural behaviour and pathogenicity for animals indicated that the organism was probably identical with *Mycobacterium balnei* described by Linell and Nordén (*Acta tuberc. scand.*, 1954, Suppl. 33). The response to the tuberculin test in 24 children who were known to be tuberculin negative before the skin lesions developed and who had never been vaccinated with B.C.G. vaccine showed that the organism could give rise to tuberculin allergy.
Benjamin Schwartz

191. **Treatment of Herpes Zoster and Chicken Pox with Immune Globulin**
J. G. RODARTE and B. H. WILLIAMS. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 553-555, June, 1956. 4 refs.

The authors report their experience at the Scott and White Hospital, Temple, Texas, of injections of γ globulin in the treatment of severe herpes zoster. The dosage advocated is 10 ml. intramuscularly into each buttock daily for at least 4 days. In none of the 11 cases so treated did severe pain recur after the first injection; sedatives were rarely needed. Early lesions failed to progress, and in all lesions there were involutionary changes. It is suggested that since post-herpetic neuralgia did not develop in any of these cases the immune globulin may minimize changes in the posterior root ganglia and spinal cord.

Immune globulin was also given to 5 children with chicken-pox, the dosage being 12 ml. on the day the eruption appeared and a similar amount on the two following days. Although the original spots were not affected, those appearing within 48 hours of the start of treatment were attenuated and new macules disappeared without causing skin damage. *E. H. Johnson*

Paediatrics

192. **Massive Pulmonary Hemorrhage in Newborn.** [In English]
E. K. AHVENAINEN. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **2**, 44–55, 1956. 13 refs.

Massive pulmonary haemorrhage of the newborn is a common finding at necropsy and is often erroneously considered to be a manifestation of haemorrhagic disease of the newborn, although the usual manifestations of neonatal hypoprothrombinaemia—such as haemorrhages from the gastro-intestinal tract—are absent in most instances. The author has analysed 60 cases of massive pulmonary haemorrhage, representing 8% of the total necropsy material examined at a children's clinic in Finland. The condition was slightly more frequent in premature than in full-term babies, and was seen most often in infants dying during the first week of life. The most common association was that with toxaemia of pregnancy. Among the associated findings in the infants, kernicterus was the most frequent and congenital heart disease the next most frequent, the latter being of the type which favours development of pulmonary congestion. There was no significant correlation with the presence of a hyaline membrane. Asphyxia, if a factor in the causation of massive pulmonary haemorrhage at all, may act indirectly through changes in the function of the heart. In none of the 60 cases was there evidence of aspiration of gastric contents. *H. S. Baar*

193. **Phthalylsulphacetamide and Neomycin in the Treatment of Infantile Gastro-enteritis**
K. B. ROGERS, R. P. BENSON, W. P. FOSTER, L. F. JONES, E. B. BUTLER, and T. C. WILLIAMS. *Lancet* [*Lancet*] 2, 599–604, Sept. 22, 1956. 1 fig., 26 refs.

The value of phthalylsulphacetamide and of neomycin in the treatment of gastro-enteritis was assessed at the Children's Hospital, Birmingham. Phthalylsulphacetamide was given by mouth in a controlled trial to several groups of healthy young adults; it caused severe gastro-intestinal disturbances and had very little effect on intestinal flora. The drug was not given therapeutically.

Neomycin was used without a controlled trial in the treatment of cases of epidemic infantile gastro-enteritis due to various strains of *Escherichia coli*, and of carriers. It was given by mouth in a fluid mixture in a dosage of 20 mg. per lb. (44 mg. per kg.) body weight, the duration of treatment varying from 4 to 13 days. There was a satisfactory clinical and bacteriological response; no toxic effects were observed and no insensitive strains were encountered. Bacteriological relapse occurred in 18% of cases, which is comparable with the relapse rate after treatment with other antibiotics, but clinical relapse occurred in only one case. It is emphasized that since very little neomycin is absorbed from the intestines any parenteral infection must be treated with another antibiotic. *Margaret D. Baber*

194. **Enuresis: a Survey of Its Treatment by the "Dri-nite" Apparatus**
W. A. DIBDEN and M. HOLMES. *Clinical Reports of the Adelaide Children's Hospital* [*Clin. Rep. Adelaide Child. Hosp.*] **2**, 247–255, May–Nov., 1955 [received Aug., 1956]. 12 refs.

The authors briefly describe the electrical "dri-nite" apparatus devised by Crosby, which stimulates the patient as soon as any urine is passed and thus awakens him, and discuss the opposing views which have been expressed concerning the use of this apparatus. They then present the previous histories and results of psychiatric examination of 26 enuretic children aged 6 to 15 years who were so treated at Adelaide Children's Hospital. After a follow-up period of 9 months to 4½ years (which they consider was probably too short in the later cases) it was ascertained that of the 26 children 11 (42%) were cured, 12 (46%) were improved but relapsed later, and 3 (12%) were unimproved. Of 19 children who had been incontinent from birth, 7 were cured; the remaining 7 of the 26 had gained temporary control but relapsed later, and of these 4 were cured. In 9 of the 11 cases of cure continence was achieved by the use of the apparatus for 4 weeks or less.

The causes of enuresis are discussed. The parent–child relationship was shown to be of extreme importance, and was good in 64% of successful treatments as compared with only 16% of the failures. The use of the apparatus did not seem to have any adverse effects on the children. It is noted that in all of these cases strict toilet training was begun during the first year and in most before the age of 6 months. *Winston Turner*

195. **Urinary Sympathin Excretion of Normal Infants and of Infants with Pink Disease**
J. W. FARQUHAR, T. B. B. CRAWFORD, and W. LAW. *British Medical Journal* [*Brit. med. J.*] **2**, 276–281, Aug. 4, 1956. 1 fig., 39 refs.

Many theories have been advanced to account for the varied clinical manifestations of "pink disease". Some of the clinical features of this disorder—which has many other names—suggest that there may be overaction of the sympathetic nervous system, and this possibility has been investigated in 4 infants with the disease seen at the Royal Hospital for Sick Children, Edinburgh, from whom, and also from 19 healthy infants, urine was collected for 24-hour periods and the excretory level of sympathin in the hydrolysed and unhydrolysed urine determined. In 3 of the 4 infants with pink disease this level was greatly in excess of normal, but in the fourth infant it was within normal limits. The authors do not claim that pink disease is the result of sympathetic overactivity, but suggest that adrenergic blocking agents may be helpful in relieving some of the clinical manifestations of the disease. *R. M. Todd*

Medical Genetics

196. **A Catamnestic Investigation of Danish Twins. A Preliminary Report**
B. HARVALD and M. HAUGE. *Danish Medical Bulletin* [*Dan. med. Bull.*] **3**, 150–158, Aug., 1956. 18 refs.

In this preliminary report from the University of Copenhagen the value of the study of twins in the field of human genetics is emphasized, comparison of the concordance of a given quality among monovular twins with that among binovular twins providing useful evidence concerning the hereditary nature of that quality. The authors show that, given reliable data, effective analysis can often be made by recourse to the simple general formula:

$$H=\frac{C_{MZ}-C_{DZ}}{1-C_{DZ}}$$

where H represents the proportion of phenotype variance attributable to hereditary factors and C_{MZ} and C_{DZ} the proportions of concordant monovular and concordant binovular twin pairs respectively. However, the difficulties of obtaining reliable unselected data are often great and these difficulties and problems of interpretation are discussed. The main purpose of the investigation here described was to compile unbiased data concerning the occurrence of certain diseases in twins in a way which could be repeated in other countries and thus provide additional material.

All twin births registered in Denmark during the years 1870–1919 were noted and by various means, including census and national registration records, legal documents, and contact with pastoral and local authorities, these twins were traced to their present address or to their death. If one or both members of a twin pair had died before the age of 5 years, both were excluded. A questionary was then sent to all living twins traced and to the nearest relatives of dead twins asking for information about all admissions to hospital and about the occurrence of a number of specific diseases. In addition information was requested about left-handedness, the number of the individual's children, and the number of twins among them. In the case of twins of the same sex, general information was requested about similarity. As a cross-check each member of a twin pair was asked about diseases experienced by the other. In all cases in which hospital admission was reported the hospital records were consulted; in cases of serious chronic disease without admission to hospital the general practitioner was consulted or the subject was seen by the authors. In the twins suffering from the conditions investigated attempts were made to confirm zygocity by blood grouping according to ABO, MNS, P, CcDEe, Lewis, Duffy, Kell, and Lutheran systems. The death certificates of dead twins were examined and necropsy reports consulted in cases of malignant disease.

Of some 9,360 pairs of twins noted in the birth registers of that part of Denmark which has been dealt with so far, about 1,900 have been completely investigated, 850 have been traced and are under investigation, 1,700 are being traced, 2,000 have proved untraceable (probably because of early death), and 2,910 have been omitted owing to the death of one or both of the members before the age of 5. A table is given showing, for each of a number of diseases, the total number of affected twins, their distribution among monovular pairs, binovular pairs of same sex, and binovular pairs of different sex, and the degree of concordance in each of these groups. The difficulties of interpreting these data and the reservations which must be made in evaluating them are discussed, and the figures for each disease or group of diseases are considered separately. [It would be unwise to quote the authors' preliminary, and often highly qualified, conclusions out of context; those interested should consult the original paper.]

As more data become available the authors propose to undertake other lines of investigation. Thus a study of discordant monovular pairs should throw some light on the environmental factors determining the disease in the affected member, while an attempt is to be made to estimate the influence of hereditary factors on the expectation of life. The authors are also collaborating with the Copenhagen University Criminological Research Institute in an investigation of twins with criminal records in the hope of gaining knowledge about the influence of hereditary factors on the social behaviour of the individual.

E. A. Cheeseman

197. **Sex-linked Hereditary Nystagmus**
J. N. LEIN, C. J. STEWART, and F. C. MOLL. *Pediatrics* [*Pediatrics*] **18**, 214–217, Aug., 1956. 15 refs.

Two families with hereditary sex-linked nystagmus are reported. In one family there were 9 males affected in 6 generations and in the other 5 males in 5 generations. The hereditary characteristic is presumably carried on the X chromosome as in red–green color blindness and hemophilia. The characteristics of the syndrome are discussed.—[Authors' summary.]

198. **Sporadic Non-endemic Goitrous Cretinism. Hereditary Transmission**
J. H. HUTCHISON and E. M. MCGIRR. *Lancet* [*Lancet*] **1**, 1035–1037, June 30, 1956. 23 refs.

The pedigree of a group of itinerant tinkers living in the West of Scotland is described among whom occurred a number of cases of non-endemic goitrous cretinism. The family is remarkable for the high degree of inbreeding which has occurred in the last 3 generations. Among 31 persons in four different sibships, 10 goitrous cretins were identified. It is concluded that the affected individuals are homozygotes for a rare autosomal recessive gene. In another sibship of 8 children 4 cases of Werdnig–Hoffmann paralysis, which is again due to the effect of a single recessive gene, were found.

H. Harris

Public Health and Industrial Medicine

199. **An Attempt at Mass Vaccination against Q Fever. I. Side-effects and Antigenicity of Q-fever Vaccine**
(Опыт массовой вакцинации против Ку-лихорадки. Сообщение 1. Реактогенность и иммуногенность Ку-вакцины)
R. I. ZUBKOVA, N. I. FEDOROVA, and N. L. KALMYKOV. *Журнал Микробиологии, Епидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 24–27, No. 7, July, 1956. 8 refs.

In the attempt at mass vaccination against Q fever here described the vaccine used was prepared from cultures of *Rickettsia burneti* grown in chick embryos, killed with formalin, and finally prepared with ether, after the method of Craigie. One ml. of the vaccine contained 1,600 million organisms. In preliminary tests on laboratory animals and human volunteers the vaccine protected guinea-pigs against 1,000 infective doses after injections of 0·25, 0·5, and 1·0 ml. at weekly intervals. Of 36 volunteers, the previously negative complement-fixation reaction had become positive in 34 within 30 to 50 days after vaccination, with titres ranging from 1 in 5 to 1 in 320.

The vaccine was then used on a larger scale in a district in the Kirghizian Republic where cases of Q fever had occurred continuously for a number of years, with occasional epidemic outbreaks; only persons with a negative complement-fixation reaction (C.F.R.) were vaccinated. In all, samples of serum from 2,310 subjects were examined and of these 342 (15%) gave a positive C.F.R., thus providing an indication of the prevalence of Q fever in the district. Of the negative reactors the comparatively high number of 1,128 subjects completed the course of three injections. General and local reactions were experienced by 39·1% after the first injection, by 62·6% after the second, and by 51·3% after the third injection. [These figures seem rather high.] However, in regard to increase of temperature alone at the three stages the corresponding figures were 4·4, 7·1, and 6·7%. The high total percentage figures for reactions were due to the inclusion of subjects showing local reactions and infiltrations, which occurred in 26 to 47·7% of the vaccinated, and headache and lassitude in 17 to 36·7%.

Five months after completion of vaccination the sera of 294 subjects were examined for C.F.R. titres. A positive reaction was obtained in 73%, the titres ranging from 1 : 5 to 1 : 640. Of these only 14·4% had titres above 1 : 160. The authors conclude that vaccination against Q fever is a practical possibility and that re-vaccination after a period of 4 or 5 months, as recommended by Meiklejohn and Lennette (*Amer. J. Hyg.*, 1950, **52**, 54; *Abstracts of World Medicine*, 1951, **9**, 110), does not appear to be necessary.

[Of a number of contributions in the same issue devoted to rickettsial infections in Russia, the above paper represents the most substantial contribution to the problems under discussion.] *K. Zinnemann*

200 (*a*). **An Epidemic of Canicola Fever in Man with the Demonstration of *Leptospira canicola* Infection in Dogs, Swine and Cattle. I. Clinical and Epidemiological Studies**
H. R. WILLIAMS, W. J. MURPHY, J. E. MCCROAN, L. E. STARR, and M. K. WARD. *American Journal of Hygiene* [*Amer. J. Hyg.*] **64**, 46–58, July, 1956. 2 figs., 36 refs.

200 (*b*). **An Epidemic of Canicola Fever in Man with the Demonstration of *Leptospira canicola* Infection in Dogs, Swine and Cattle. II. Laboratory Studies**
M. K. WARD, M. B. MCDANIEL, H. W. TATUM, L. E. STARR, and H. R. WILLIAMS. *American Journal of Hygiene* [*Amer. J. Hyg.*] **64**, 59–69, July, 1956. 17 refs.

These two articles from the Georgia State Department of Public Health and the U.S. Public Health Service concern an outbreak of infection with *Leptospira canicola* during the summer of 1952 in a small, isolated settlement outside the city of Columbus, Georgia, in which 24 laboratory-confirmed cases of canicola fever occurred among the 141 residents and 2 additional cases among non-residents.

The first article deals with the epidemiological and clinical aspects. The settlement consisted of 30 one-storey buildings, with very primitive sanitation, surrounded by fields used for the pasturing of cattle, pigs, a mule, and a horse. In June, 1952, a small swimming pool had been formed by damming a stream running through the pasture and used by the farm animals for water, and leptospirosis was first suspected when it was learned that all the affected persons, without exception, had been swimming in the pool, whereas none of the residents who had had no contact with the pool were affected. Of 55 persons known to have used the pool, at least 26 became infected, and the attack rate appeared to be highest among those who bathed most frequently and whose activities included diving and immersion of the head and mouth. The clinical picture observed is described, and differed from the classic descriptions mainly in the absence of jaundice and renal involvement. With one doubtful exception, all the patients recovered without relapse or later complications. Serological tests carried out on blood from a number of animals gave positive reactions not only in dogs, but also in cattle and pigs which had access to, and were presumably infected from, the stream.

This is the largest outbreak of canicola fever yet recorded in the U.S.A., where not more than 50 cases have been reported since 1938, when it was first diagnosed in that country. It is of particular interest in that it provided evidence that *L. canicola* infection can occur in animals other than dogs and man, and that the infectivity rate for man is high among those exposed to the organism in swimming pools.

The laboratory studies carried out in connexion with this outbreak, involving the examination of blood and

urine by culture methods and by inoculation into 19- to 21-day-old hamsters, are described in the second paper. A modified form of Korthof's medium was found to be the most satisfactory for culture purposes, and details of its preparation are given. Sera were tested against type strains of *L. icterohaemorrhagiae*, *L. canicola*, and *L. pomona*, both living and formalinized antigens being used for the agglutination tests. The agglutination titre generally rose to a maximum of 1:1,000 or 1:2,000 between the second and fourth weeks after onset, but occasionally very much higher titres, up to a maximum of 1:128,000, were observed. It was noted that the complement-fixation reaction was positive only with sera which had been collected during the first 3 weeks of the illness.

Of 7 cultures of blood from infected persons, only one was positive, and of 17 hamsters inoculated with urine from 13 infected patients, *L. canicola* was recovered from the heart blood of one only; this animal had been inoculated with urine obtained on the 34th day of illness. The organism was also recovered from 3 hamsters inoculated with urine from dogs and from one hamster inoculated with an emulsion of kidney tissue from a pig. Each of the 6 strains isolated (2 human, 3 dog, and 1 pig) was tested with antisera against 16 type strains of *Leptospira* and showed cross-agglutination patterns similar to those of *L. canicola*. Antisera prepared against each of the 6 isolates agglutinated all the others to the full titre of the homologous organism. This is the first time that the isolation of this species from the pig has been reported, and the serological tests provided the first evidence that *L. canicola* may also occur in cattle.

Edward Hindle

201. **An Apparently Water-borne Outbreak of Infectious Hepatitis**

A. PECZENIK, D. W. DUTTWEILER, and R. H. MOSER. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **46**, 1008–1017, Aug., 1956. 2 figs., 4 refs.

Epidemiological details are given of an outbreak of infective hepatitis in a group of members and employees of the United States Army and other organizations in Austria.

Between February 24 and March 15, 1955, 10 frank cases of infective hepatitis were diagnosed clinically and 6 others on laboratory evidence, all 16 patients having participated in skiing trips to Bad Gastein in January—15 of them in an organized party of 82 persons and one independently. All but one of the patients had stayed at the same hotel (together with 54 other members of the party) and the remaining patient had eaten at least one meal at this hotel although staying elsewhere.

Preliminary investigation having thus shown the possibility of a common origin, the hotel was inspected. The kitchen equipment and food-handling practice proved to be extremely poor, and specimens of food, including the milk supply, were found to be grossly contaminated with *Escherichia coli* and staphylococci. A search for a source of infection among food-handlers was unsuccessful, 2 hotel employees who had developed infective hepatitis on February 15 and March 6 respectively being considered to have been infected from the same source as the American patients. The hotel drew most of its water from the municipal system, which was satisfactory, but " utility " water (for water-closets and similar purposes) came from a private source and it was found that the two systems were interconnected. Specimens of drinking water and " utility " water drawn within the hotel were tested and both were found to be heavily contaminated with coliform organisms. The source of " utility " water was a reservoir fed by a pipeline from mountain springs and lying 122 feet (37 m.) from, and 20 feet (6 m.) below a septic tank serving another hotel, the pipe carrying the effluent from the septic tank crossing the supply pipe to the reservoir. The reservoir was in poor condition and *E. coli* was found in all dilutions of samples of its water examined bacteriologically. It was then found that a guest who had stayed at the other hotel from January 17 to 30 had developed infective hepatitis on January 21. In view of these findings the authors [not unnaturally] conclude that the outbreak was waterborne.

[On the assumption that the guest at the other hotel was the primary source of infection, the incubation period was between 25 and 40 days. Bearing in mind that it was winter in the Austrian alps, with day and night temperatures below 0° C., and that the virus presumably resided for some time in both septic tank and reservoir, this period is unusually brief. It should also be noted that it is stated that 7 out of 26 persons who had eaten cream during their stay at Bad Gastein developed infective hepatitis, and that both patrons and employees of the first hotel had been treated frequently for diarrhoea during the preceding 2 years.] *W. K. Dunscombe*

202. **Efficacy of Trivalent Adenovirus (APC) Vaccine in Naval Recruits. Progress Report**

J. A. BELL, M. J. HANTOVER, R. J. HUEBNER, and C. G. LOOSLI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 1521–1525, Aug. 18, 1956. 8 refs.

The preliminary results are reported of a combined study by the National Institutes of Health, Bethesda, Maryland, the University of Chicago, and the U.S. Naval Medical Research Unit of the effects on 4,000 naval recruits of the administration of a formaldehyde-inactivated vaccine of adenovirus (A.P.C. or A.R.D. viruses) containing Types 3, 4, and 7, which was injected intramuscularly in a single 2-ml. dose without untoward local or general reactions. A control group of 12,000 men was also studied.

Blood samples taken before and 14 and 28 days after vaccination were examined for neutralizing antibodies against all three types of virus in HeLa-cell cultures and in monkey kidney-cell cultures. The monkey kidney-cell technique was more sensitive in defining the end-point of delayed development of cytopathogenic effects than the HeLa-cell test. The vaccine induced a substantial rise in the titre of serum antibodies to each of the three virus types. A concurrent rise in the titre of similar serum antibodies in some of the control subjects who

received a placebo was attributed to heterotypic responses or to undetected natural infection.

On comparison of the incidence of acute respiratory illnesses among the vaccinated and non-vaccinated recruits no significant difference was found in respect of minor afebrile attacks, but among the vaccinated recruits the incidence of febrile illnesses and of illnesses requiring admission to hospital was significantly lower. A substantial proportion of the febrile respiratory infections were due to Type-4 virus, and illnesses due to Types 3 and 7 were not prevalent during the period of observation. A protective effect of vaccination can therefore be claimed against Type-4 adenovirus infection only. *D. Geraint James*

203. **Comparison of Coliform Group Organisms with Enterococci from Well Waters**
C. RITTER, I. F. SHULL, and R. L. QUINLEY. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **46**, 612–618, May, 1956. 14 refs.

In an investigation carried out by the Kansas State Board of Health a study was made of the relative value of enterococci and coliform organisms as indicators of faecal pollution of well waters. One sample of water from each of 595 wells in rural Kansas was examined for coliform bacteria by the standard method of the American Public Health Association (lactose broth, with confirmation in brilliant-green–bile) and for enterococci by inoculation into the azide–dextrose broth of Rothe, with confirmation of positive samples by transfer to crystal-violet–azide broth. The enterococci were further identified by morphology, by their strong reducing abilities, and by their ability to grow at 45° C. and *p*H 9·6 and also in the presence of 0·1% methylene blue or 6·5% sodium chloride.

There was a close correlation between the presence of coliform bacteria and enterococci in the samples examined. The authors stress, however, that in such tests the finding of atypical enterococci is as important as that of *Streptococcus faecalis*. The chief value of examining for enterococci is when coliform contamination of the water is found to be fluctuating or of a low order. *R. Hare*

INDUSTRIAL MEDICINE

204. **Byssinosis in Cotton and Other Textile Workers**
R. S. F. SCHILLING. *Lancet* [*Lancet*] **2**, 261–265 and 319–325, Aug. 11 and Aug. 18, 1956. 11 figs., bibliography.

Byssinosis, a chronic respiratory disease caused by the inhalation of cotton, flax, and hemp dust, has been recorded among textile workers in Great Britain for over 200 years. The condition is characterized by breathlessness associated with tightness of the chest and a short, dry cough, particularly on returning to work on Mondays. In the initial stages the symptoms disappear on leaving the mill, but as time goes on they become more severe and continuous and cause disablement for work. The workers mainly affected are those employed in dusty processes, particularly the strippers and grinders in the card rooms and workers in the blow-rooms of cotton mills. The first serious study of the problem was carried out in 1909 by Collis, who recorded that of 126 strippers and grinders from mills in Blackburn, 93 (74%) had the characteristic asthmatic complaint on Mondays and 51 of these were severely affected. However, 6 years later he suggested that, owing to improved methods of dust control, the disease was rapidly disappearing. This conclusion was supported by other observers and by Home Office committees in 1932 and 1939.

For a variety of reasons statistical information on mortality and morbidity among cotton workers in the past is unreliable. Thus in the reports of the Registrar-General before 1910 the separate occupations of cotton workers were not differentiated, making comparison between the mortality in dusty and non-dusty trades impossible. Again, up to 1939, any cardiovascular disease was regarded as the cause of death in preference to any respiratory disease where both were mentioned on the same certificate, so that many deaths primarily due to respiratory disease were classified under cardio-vascular–renal disease, which was therefore regarded as the more important risk for card-room and blow-room workers.

In field studies carried out by the author and others in 1948–9 in Lancashire cotton mills card-room strippers and grinders and blow-room workers aged 50 to 59 were found to have a significantly higher average blood pressure than the weavers, though the number who had hypertension was too small to suggest that this was a serious occupational risk. On the other hand a very high prevalence of chronic respiratory disease was found among middle-aged card-room and blow-room workers. Attention was thus drawn again to byssinosis and the problem of its differentiation from non-occupational bronchitis, which is very prevalent among the general population in the Lancashire cotton towns. A survey made in 1953 showed the occurrence of Monday symptoms, particularly tightness of the chest, to be the critical diagnostic feature of byssinosis, and the extension of the symptoms to other days as the disease progresses has been found to provide a reliable basis for the classification of cases in two grades of severity. Epidemiological studies in various types of mill and at various locations in individual mills proved that work in mills spinning the coarser grades of cotton was more harmful to the workers than the same work in mills dealing with the finer grades, and that the nearer the work position was to the carding engines, the higher was the prevalence of respiratory disease. The occurrence of byssinosis has been reported among workers in the cotton industry throughout the world, and the same or a similar condition has been observed among workers exposed to the inhalation of other vegetable dusts, notably flax and hemp.

The pathology of byssinosis has not as yet received close study and the appearances are usually described as those of chronic bronchitis and emphysema. However, Gough has reported to the author the presence in the lungs in 3 cases of byssinosis of " bodies " comparable to asbestosis bodies but different in shape, while a relatively

minor degree of emphysema appears to be characteristic of the disease. Although various hypotheses have been advanced to explain the pathogenesis of the disease and the occurrence of " Monday symptoms ", none is wholly acceptable, and there is need for further research to elucidate the problems of chronic respiratory disease in the cotton and other textile industries. In the meantime preventive measures are urgently called for and these primarily involve the determination of permissible levels of dust concentration. The periodical medical examination of textile workers and the removal from risk of those showing early signs of byssinosis is recommended.

[This paper constitutes the text of the Milroy Lectures delivered before the Royal College of Physicians of London on February 7 and 9, 1956, and, together with previous reports by the author and his co-workers, constitutes the most complete and authoritative account of byssinosis to date.] *A. Meiklejohn*

205. **Methods of Purification of Effluents Containing Phenols.** (О способах очистки фенольных сточных вод) N. O. Grigoruk. *Гигиена и Санитария* [*Gigiena*] 8–14, No. 7, July, 1956. 1 fig.

The removal of phenols from tar distillation plant effluents may be effected by a biochemical process, using pure cultures of bacteria grown in phenolic media, or by a biological process using activated sludge. Conditions favouring the biochemical process are: (*a*) preliminary removal of sediment, especially tar and oil, (*b*) an abundant supply of oxygen, (*c*) the presence of phosphorus, (*d*) *p*H between 7 and 9, and (*e*) constant temperature.

This method was adopted at the Kadyev tar distillation works in 1951 to deal with 17 c. m. of effluent per hour with a phenol content averaging 2,000 mg. per litre. After passing through an oil separator and coke pressure filter the effluent is treated with 0·2 to 0·5 kg. of superphosphate per c. m. and then enters the biological tank, in which it is exposed to the action of phenol-decomposing bacteria. After purification the effluent either circulates again through the tank to dilute the fresh liquid to about 1 in 100 as it enters, or leaves the biological tank to pass through a settling tank and finally, after mixing with other sewage, is discharged into a river.

In practice, this biochemical plant proved very successful in removing not only phenols but other impurities too, as shown by the reduction in the oxygen absorption of the effluent. The river water remained satisfactory. A difficulty arose, however, in the biological tank, where the development of a slime, composed mainly of tar and oil, interfered with the biochemical process and led ultimately to the suggestion that an activated-sludge process should be substituted.

The author, opposing this suggestion, postulates the following requirements for the successful operation of activated sludge: (*a*) biochemical oxygen demand not greater than 20 mg. per litre, (*b*) presence of nitrites to give 8 to 10 mg. of nitrogen per litre, (*c*) phenol content up to 1 mg. per litre, (*d*) absence of smell from chlorination, (*e*) 10,000 colonies of bacteria per ml., and (*f*) not more than 30 mg. of total solids per litre. In practice, it is also necessary to dilute the effluent containing phenols up to 10 to 15 times before treatment. This rules out the method in industrial areas where water is scarce. *Basil Haigh*

206. **Industrial Hygiene Problems in the Manufacture of Benzanthrone.** (Вопросы гигиены труда при производстве и применении бензантрона)
V. G. Piskunova, V. S. Anatovskaya, G. D. Korotkova, A. B. Nerubenko, V. I. Danilov, M. I. Érman, and Z. I. Eremina. *Гигиена и Санитария* [*Gigiena*] 22–26, No. 7, July, 1956.

Benzanthrone is an aromatic ketone from which is derived a series of complex dyes. Evidence of its toxicity has been found among workers at a factory in the Ukraine where it is manufactured from anthraquinone and glycerine. During the course of manufacture, especially during the processes of sublimation and final crushing, workers are exposed to benzanthrone dust, in concentrations as high as 3,570 mg. per litre, which may be absorbed by the skin or respiratory tract. Toxic effects were also noted, however, among workers not exposed to such high concentrations of dust.

The first manifestations of toxicity were usually found during the first or second year of exposure, but occasionally as early as the third week. The skin was affected first, erythema and oedema being followed after a few weeks by merging patches of pigmentation and atrophic changes. Loss of appetite and weight and a lowering of the basal metabolic rate were consistently found. Complaints of pain in the epigastrium and right hypochondrium were frequent, and moderate enlargement of the liver together with abnormal results of liver function tests indicated the presence of toxic hepatitis. Chronic gastritis and myocarditis were occasionally found. Effects on the nervous system included diminution of reflexes and signs of sympathetic dystonia. Acetylcholine appeared in the blood during the stage of development of the toxic manifestations.

The natural course of the disease is to become chronic and then slowly to regress, although the pigmentation rarely diminishes. Treatment with nicotinic acid, aneurin, ascorbic acid, glucose, and insulin, and with either stimulants or sedatives of the central nervous system, has been advised. Prophylactic measures include the mechanization of dusty jobs, improvement of ventilation, and the use of airtight containers for transport of benzanthrone. *Basil Haigh*

207. **Advances in Industrial Toxicology for the Year 1955**
H. E. Stokinger. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **14**, 206–212, Aug., 1956. 24 refs.

208. **Pneumoconiosis in Textile Spinners.** (Les pneumokonioses des filatures)
J. P. Lemercier and —. Manouvrier. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **17**, 443–449, Sept.–Oct., 1956. 28 refs.

Forensic Medicine and Toxicology

209. **Hemodialysis, an Effective Therapy for Acute Barbiturate Poisoning**
L. B. BERMAN, H. J. JEGHERS, G. E. SCHREINER, and A. J. PALLOTTA. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 820–827, June 30, 1956. 10 figs., 20 refs.

Of 26 patients admitted to Georgetown University Hospital, Washington, D.C., suffering from acute barbiturate poisoning, 8 who were severely ill were treated by blood dialysis, a Kolff dialyser as described by Kyle *et al.* (*J. clin. Invest.*, 1953, **32**, 364; *Abstracts of World Medicine*, 1953, **14**, 433) being used. There were 2 deaths due to other pathological conditions. The remaining 6 patients recovered, although the initial blood concentration of barbiturate was exceedingly high, reaching 29 mg. per 100 ml. in one case. The blood barbiturate level was determined every hour during treatment, and it was found that the percentage of barbiturate dialysed into the bath was at first proportional to the blood concentration of the drug, but usually increased as the patient's general condition improved.

The authors consider that in severe cases recovery is more rapid with blood dialysis than with other methods of treatment and the risk of pulmonary complications is thus reduced. All the patients in the present series were completely comatose and had no corneal reflex.

V. J. Woolley

210. **Hepatic Pathology in Jaundice Due to Chlorpromazine**
A. A. STEIN and A. W. WRIGHT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 508–511, June 9, 1956. 2 figs., 8 refs.

The pathological changes in the liver in patients treated with chlorpromazine are described in this paper from Albany Medical College and Albany Hospital, New York, with special reference to 4 cases of jaundice due to this drug, 3 of which were examined post-mortem and one at exploratory laparotomy. In the 3 fatal cases the jaundice was associated respectively with an intracranial tumour, severe chronic renal disease, and diabetes with gangrene. The clinical and pathological findings are described in detail. In 2 cases the liver was examined when the jaundice was at its height, and the changes were seen to be primarily those of central degeneration of the liver cells, with bile stasis and local pigment deposits similar to those present in moderately severe obstructive jaundice. In the third case the changes were less severe, and in the fourth, where the jaundice had disappeared, the liver showed only minimal changes, suggesting that it had sustained little or no permanent damage. In none of the cases was there any evidence of organic obstruction in the extrahepatic biliary tract. Comparison of the histological appearances of the liver in these cases with those in obstructive jaundice showed no definite distinguishing features unless the extrahepatic obstruction had been very severe. In one case the jaundice cleared rapidly after administration of cortisone and the patient recovered.

The authors suggest that chlorpromazine may in some way act on the bile, causing an alteration in its composition followed by increased viscosity or actual inspissation, and that in this case the effect of cortisone would be to reduce the viscosity of the bile. They compare the condition with the so-called inspissated-bile syndrome in children.

P. N. Magee

211. **The Treatment of Carbon Monoxide Poisoning with Cytochrome.** (Traitement de l'intoxication oxycarbonée par le cytochrome)
J. F. GROS and P. LÉANDRI. *Presse médicale* [*Presse méd.*] **64**, 1356–1357, July 28, 1956. 3 refs.

Cytochrome C is known to play an important part in biological oxidation–reduction processes, and has been used successfully in the treatment of carbon monoxide poisoning in Germany. The present authors describe the results obtained in 20 out of the several thousand cases of carbon monoxide poisoning from various causes treated each year by the Medical Service of the Paris Fire Brigade.

Cytochrome was given intravenously in a single dose of 15 or 30 mg., repeated if necessary a quarter of an hour later. Consciousness usually returned within 8 to 15 minutes, cyanosis became less, respiratory efficiency improved, and the reflexes returned to normal. Adjuvant therapy consisted in the administration of oxygen and a cardiac stimulant (usually either nikethamide or ouabain). All the patients were revived, though 2 subsequently died from secondary complications. Although the effectiveness of cytochrome varied in different patients (presumably because of different degrees of poisoning) the authors found that with its help resuscitation was achieved more rapidly.

R. Wien

212. **The Study of Human Hairs as an Aid to the Investigation of Crime**
D. N. JONES. *Journal of Forensic Medicine* [*J. forensic Med.*] **3**, 55–63, April–June, 1956. 14 figs.

Present knowledge concerning the medico-legal value of the identification of human hair is reviewed, with illustrative cases. The effect of stretching the hair is discussed; it is pointed out that this reduces the mean diameter on cross-section and may lead to the mistaken inference that two samples did not come from the same source. The author found by experiment that the degree to which different samples could be stretched and consequently altered in diameter varied considerably from case to case.

Gilbert Forbes

Anaesthetics

213. **Value of Chlorpromazine in Preoperative Medication**
W. A. Weiss, J. P. McGee, J. O. Branford, and E. C. Hanks. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **161**, 812–815, June 30, 1956. 4 refs.

Chlorpromazine was given in combination with other drugs in the preoperative medication of 725 patients, the patients being divided into four groups, each of which received a different combination of drugs with chlorpromazine. The proportion of satisfactory results in these four groups varied between 80 and 87%. [Not only were other central depressants administered as well as chlorpromazine, but there was no control group and the results were not tested for significance.] Complications, such as tachycardia, hypotension, and nasal congestion, which were attributed to the premedication, were noted in 28·5% of the cases. *Ronald Woolmer*

214. **The Etiology and Treatment of Laryngeal Spasm**
B. R. Fink. *Anesthesiology* [*Anesthesiology*] **17**, 569–577, July–Aug., 1956. 7 figs., 4 refs.

In this paper from the Presbyterian Hospital (Columbia University), New York, the author first outlines evidence recently brought forward which shows that both a shutter and a ball-valve mechanism are involved in the closure of the larynx. The thyroid cartilage and hyoid bone are drawn together, the vocal and false cords are approximated, and the intralaryngeal part of the epiglottis presses down on top of these to make a tight fit. This movement obliterates the vestibule and ventricle of the larynx, and is accompanied by electrical activity in the thyrohyoid, sternohyoid, and sternothyroid muscles.

He then discusses various types of laryngeal obstruction occurring during general anaesthesia in relation to this mechanism. Expiratory glottic stridor occurs when somatic sensory stimulation occurs during light anaesthesia, causing adduction of the vocal cords independently of the ball-valve mechanism, and may be abolished either by deepening anaesthesia or removing the stimulus. Inspiratory glottic stridor occurs as a result of paralysis of the abductor muscles from deep anaesthesia or other causes, the negative pressure during inspiration sucking the cords together. This is aggravated by deeper respiration, and may be abolished by reducing the depth of anaesthesia until abductor tone returns or by applying positive pressure during inspiration.

These two forms of obstruction are partial only, are due to malfunction of the intrinsic muscles of the larynx, and are readily treated. When the ball-valve mechanism is involved, however, as by direct stimulation of the laryngeal mucosa, complete closure is produced with the aid of the extrinsic muscles and forced inflation distends the piriform fossae, closing the glottis still more firmly. Lifting the jaw may help to relieve such spasm by pulling the hyoid bone upwards, but removal of the stimulus, deepening anaesthesia, or the use of relaxants may be necessary. *Raymond Vale*

215. **Ventricular Fibrillation during Hypothermia Successfully Treated by Rewarming and Electroshock**
E. Husfeldt and O. Secher. *Thorax* [*Thorax*] **11**, 67–70, June, 1956. 2 figs., 11 refs.

The literature on the prevention and treatment of ventricular fibrillation during hypothermia is briefly reviewed, and the authors point out that all authorities are agreed that if such a complication should occur rewarming must be carried out as quickly as possible, because defibrillation has been found to be easier at normal body temperature.

In 3 cases of ventricular fibrillation here described from the Rigshospital, Copenhagen, surface cooling was employed after induction of anaesthesia. The rectal and oesophageal temperatures were recorded, and electrocardiograms obtained at intervals. The type of anaesthesia varied slightly in the 3 cases, but all the patients were intubated and hyperventilated. In the first case, in a 17-year-old girl undergoing operation for repair of an atrial septal defect, ventricular fibrillation began immediately after closure of the defect. Cardiac massage, various injections, and electric shock were all ineffective until 125 litres of hot (40° C.) saline solution was poured into the thoracic cavity, whereupon the oesophageal temperature rose from 26° to 34·2° C.—the rectal temperature remaining constant at 27° C.—and on electrical stimulation the heart regained normal rhythm after being in fibrillation for 1 hour 54 minutes; there were no untoward sequelae. The other 2 cases occurred during operations for isolated stenosis of the pulmonary valve in patients aged 10 and 20. In both cases fibrillation began when the circulation was interrupted to allow an open repair. Attempts at defibrillation by the usual methods proving unsuccessful, 65 litres of hot saline in one case and 150 litres in the other was introduced into the thoracic cavity. Fibrillation was arrested when the oesophageal temperature reached 32·4° and 35·2° C. respectively. In the first of these cases, in which fibrillation was present for 50 minutes, recovery was uneventful, but in the second fibrillation had lasted for 109 minutes and the patient's mental state was still abnormal 14 days later.

The authors suggest that these results justify rapid rewarming when defibrillation is ineffective at low body temperatures. They point out that the rectal temperature did not begin to rise until normal heart rhythm was restored, and it therefore seems likely that the oesophageal temperature is a surer guide to the temperature of the heart and to the progress of the treatment of fibrillation. *D. D. C. Howat*

Radiology

216. **Cushing's Disease: Its Roentgenographic Findings**
C. C. WANG and L. L. ROBBINS. *Radiology* [*Radiology*] 67, 17–25, July, 1956. 12 figs., 10 refs.

The authors present an account of the radiological findings in 38 cases of Cushing's disease seen at Massachusetts General Hospital (Harvard Medical School), Boston. In addition to the well-known spinal osteoporosis in this condition osteoporosis was also seen in the pelvis and ribs, while the extremities were similarly involved in 7 cases. Mention is also made of stippled osteoporosis of the skull in 13 patients, the appearance being similar to that observed in hyperparathyroidism. Signs of multiple fractures of the ribs were seen in 14 cases and were characterized by abundant callus. Calcification of the aorta and its branches unusually early in life occurred in 4 cases, but nephrocalcinosis was not seen in the series, although 13 patients had renal calculi. The authors recall that some patients receiving treatment with cortisone or ACTH may develop iatrogenic Cushing's disease and manifest similar changes. They point out that the findings described are not specific for Cushing's disease but, taken together with the clinical findings, may lead to the correct diagnosis.

D. E. Fletcher

217. **Roentgenographic Manifestations of Congenital Peripheral Arteriovenous Communications**
T. O. MURPHY and A. R. MARGULIS. *Radiology* [*Radiology*] 67, 26–33, July, 1956. 8 figs., 11 refs.

Peripheral arterio-venous communications—the so-called " glomus bodies "—are present normally in man and are concerned in the regulation of body heat. Occasional cases of maldeveloped glomus bodies with numerous arterio-venous communications are seen, however, and 8 examples have been examined by femoral arteriography at the University of Minnesota Hospitals, Minneapolis. The technique of demonstration is described and a number of characteristic radiographs are reproduced.

Venous retia—that is, plexiform collections of distended veins—were seen, usually near the ankle, in 7 of the patients; in these, venous filling occurred at the same stage as arterial filling and included the deep venous system through large shunts. Segmentation of arterial branches, coming off the parent vessel in a regular and periodic pattern, was another feature noted. In some cases a vessel was observed running parallel to the deep artery and connected to it by a transverse vessel to produce an H-shaped formation, which was presumably the communication itself. Finally it is noted that the smaller peripheral vessels did not taper as they do normally and seemed to be under little or no neuromuscular control. The condition is difficult to diagnose and it is suggested that it may be more frequent than is generally realized.

D. E. Fletcher

218. **Intracardiac Angiography: Controlled Instantaneous Intra-atrial Release of Contrast Material in Man**
B. L. BROFMAN. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] 32, 28–34, July, 1956. 3 figs., 11 refs.

A method whereby contrast material may be liberated suddenly into the right atrium is described in this paper from the Mount Sinai Hospital, Cleveland, Ohio, which, it is claimed, is without ill effects and gives excellent visualization of the right ventricle and its outflow. A double-lumen No. 9 catheter is used, one lumen of which is connected by a stainless steel tube to a short single-lumen catheter with a blind end and a side aperture 5 to 6 cm. above it. A latex balloon, its proximal end securely held by a tight rubber cuff, surrounds this catheter; thus when 40 to 50 ml. of 70% diodone is injected it passes through the side opening and inflates the balloon. Two silk ligatures tied to the connecting tube pass distally between the cuff and the neck of the balloon, their free ends being attached to the end of a stainless steel wire passed along the second lumen of the double catheter. Sudden tension on this wire causes the rubber cuff to be rolled upwards, freeing the neck of the balloon and so releasing the contrast medium. This technique has been used satisfactorily in 5 cases.

(It is noted in an addendum that a method using a single-lumen catheter and a simplified release mechanism has now been devised which has been used without ill effects in 25 cases.)

H. E. Holling

219. **The Roentgen Diagnosis of Herniated Disk with Particular Reference to Diskography (Nucleography)**
W. G. PEACHER and R. P. STORRS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 76, 290–302, Aug., 1956. 15 figs., bibliography.

In the opinion of the authors myelography is still a very useful procedure in the diagnosis of lesions of the intervertebral disks if carefully performed, but it is emphasized that errors in interpretation will continue to occur if an inadequate amount of contrast medium is used, an insufficient number of films taken, or if exploration of the vertebral canal is incomplete. The average amount of contrast medium needed is 6 ml., but the authors state that as much as 24 ml. may be used. [This seems to be an excessive amount, unless adequate removal can be ensured.] The advantages of myelography are that it allows the entire spinal canal to be visualized, that it is of value in differentiating tumours from disk protrusion, and that it indicates the presence of multiple lesions. " Pantopaque " is less irritating than " lipiodol " and is more easily removed, but its absorption rate is very slow (1 ml. per annum) if it is not removed.

Diskography is of additional value when a bulging annulus is observed, and is useful in demonstrating the

amount of disk degeneration present. It is also of value when myelography is negative and in the diagnosis of atypical back pain and sciatic syndromes. It should not be performed when rupture of the disk has occurred, as there is then a greater risk of local nerve-root injury due to distortion of the cauda equina, while severe local symptoms may result from the extradural extravasation of the contrast medium used (diodone) if there is an opening through the annulus fibrosus. The authors do, however, recommend diskography in cases of long-standing low back pain as a means of demonstrating possible underlying degenerative disk disease with or without mild protrusion not visible in the myelogram. They advise initial investigation by myelography, which, they say, will give positive findings in over 90% of cases with a typical clinical history and objective neurological signs. In cases in which the myelographic findings are equivocal or negative, the history atypical, the physical and neurological signs negative or minimal, and the response to treatment unsatisfactory diskography is recommended.

J. MacD. Holmes

220. **Splenoportography: a Valuable Adjunct in the Study of Portal Hypertension**

H. F. RODRIGUEZ, F. H. GARDNER, and R. DIAZ-BONNET. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **232**, 1–7, July, 1956. 5 figs., 5 refs.

Splenoportography is a relatively simple procedure and is used as a routine on all patients with portal hypertension selected for surgery at the District Hospital, Bayamon, Puerto Rico. Schistosomiasis involving the liver is prevalent in Puerto Rico, and often leads to portal hypertension with the development of gross splenic enlargement and oesophageal varices. The procedure of splenoportography is as follows. After a sensitivity test with diodone the injection site is infiltrated with 1% amethocaine hydrochloride to the peritoneal surface. When splenomegaly is present the contrast medium is injected into the spleen with a 3-inch (7·6-cm.), 18-gauge needle in the anterior axillary line below the costal margin. The patient is instructed to hold his breath and the needle is inserted upwards and medially at an angle of approximately 45 degrees. If the spleen is only slightly enlarged the diodone is injected through the left ninth intercostal space in the midaxillary line. The injection of 20 to 30 ml. of 70% diodone is given rapidly, and as the last 5 ml. is injected an anteroposterior radiograph is taken.

Splenoportography was carried out on 35 occasions in a series of 26 patients, 28 satisfactory radiographs being obtained. Untoward effects were limited to a feeling of warmth, nausea, and headache, though in 6 cases there was some left upper quadrant pain for a short period. In 10 of the cases operation was performed shortly afterwards, and in one of these there was about 150 ml. of blood in the peritoneal cavity, but the site of the haemorrhage had been sealed off.

The appearances after splenoportography in healthy subjects, in various pathological states, and after the operation of porta-caval shunt are described. The procedure is of value for studying portal hypertension and for assessing the need for shunt anastomosis and the results of operation. In 2 cases the presence of varices was demonstrated when a radiograph taken after a barium swallow was normal.

Sydney J. Hinds

221. **Percutaneous Transhepatic Cholangiography**

J. REMOLAR, S. KATZ, B. RYBAK, and O. PELLIZARI. *Gastroenterology* [*Gastroenterology*] **31**, 39–46, July, 1956. 12 figs., 10 refs.

Percutaneous transhepatic cholangiography was attempted on 34 patients at the Policlinico de Lanus, Buenos Aires, the technique, which was in the main similar to that previously described, being as follows. The puncture was made with an 18-gauge, 6-inch (15·2-cm.) needle two fingerbreadths below and 2 cm. to the right of the xiphoid process, local analgesia being obtained with 2% procaine. The needle was directed slightly to the right and upwards to a depth of approximately 12 cm., and then slowly withdrawn until bile was obtained. The greatest possible quantity of bile was withdrawn, and 35% diodone was introduced under fluoroscopic control, 20 ml. of the medium being usually sufficient, although up to 60 ml. was necessary in some cases. Radiographs were taken and barium was given by mouth. Before the needle was removed as much diodone as possible was withdrawn again. The authors state that they have not had any accidents with this method but that intra-abdominal haemorrhage and choleperitoneum are possible complications. Filling of intra- and extra-hepatic biliary channels was achieved in 20 of the 34 patients.

As a result of their investigations the authors have come to the conclusion that the enlargement of the intrahepatic bile ducts caused by benign processes is greater than that caused by carcinoma. In their view percutaneous transhepatic cholangiography is indicated: (*a*) in doubtful cases of jaundice where laboratory tests are inconclusive; (*b*) to differentiate lithiasis from a neoplasm in the aetiology of jaundice; and (*c*) in the post-cholecystectomy syndrome with jaundice.

John H. L. Conway-Hughes

RADIOTHERAPY

222. **Lymphatic Dissemination of Radiogold in the Presence of Lymph Node Metastases**

C. G. THOMAS. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **103**, 51–56, July, 1956. 6 figs., 2 refs.

Since it has been suggested that radioactive gold (^{198}Au) injected in the vicinity of a tumour might be carried to the lymph nodes for the successful irradiation of metastases there, the author, at the University of North Carolina, decided to investigate this possibility experimentally.

Colloidal ^{198}Au, with a particle size of 50 to 100 millimicrons, was diluted with 1% solution of procaine to provide a specific activity of 0·1 to 5·0 millicuries per millilitre. Preliminary trials indicated that an injection containing 0·5 to 1·0 millicurie was sufficient. Radical removal of the primary tumour and regional

lymph nodes was carried out within 20 to 24 hours, or in a few cases after a somewhat longer interval. All the lymph nodes were carefully dissected out and their location plotted on a diagram. The radioactivity of each node was determined with a gamma-sensitive Geiger counter. Dark-field examination of the tissue sections disclosed the location of the ^{198}Au, which appeared as highly refractile spherical or cylindrical bodies.

This technique was employed in 23 cases of carcinoma of the breast and 12 of carcinoma originating in the head and neck. In all, 593 lymph nodes were examined. It was found that where no metastatic invasion of the lymph nodes had occurred the ^{198}Au became diffused evenly throughout the whole group of nodes. The presence of metastases, however, profoundly disturbed this even distribution. In the nodes actually involved by cancer the retention (by phagocytosis) of ^{198}Au was inversely proportional to the amount of malignant tissue present. The author concludes that since the effective tissue penetration of the predominant ray (beta) in tissue is only 0·5 of a millimetre, satisfactory irradiation of lymph-node metastases cannot be obtained in this way.

E. Stanley Lee

223. **Radioactive Gold in the Treatment of Ovarian Carcinoma**

H. B. Elkins and W. C. Keettel. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 1117–1123, June, 1956. 2 figs., 5 refs.

Since January, 1952, cytological studies of peritoneal washings have been performed at the State University of Iowa College of Medicine, Iowa City, on all gynaecological patients undergoing abdominal surgery. The peritoneal cavity is washed out with 15 to 20 ml. of saline solution which is then centrifuged and the sediment treated with Papanicolaou's stain.

In a series of 275 such patients benign ovarian tumours were found in 35 cases (there was one false positive smear), and of 20 others later shown to have ovarian carcinoma, the smear test in 13 gave either positive or suggestive evidence of malignancy. The authors state that " 5 positive smears occurred in a group of 10 patients who showed no break through the ovarian capsule, and no evidence of neoplasm outside the ovary ", from which they conclude that the presence of free malignant cells floating in the abdominal cavity even in the early stages of ovarian carcinoma is established. They classify the extent of the disease in their patients by a modification of Heyman's system, for details of which the original paper should be consulted.

Since 1951, 66 patients have been treated with radioactive gold (^{198}Au) injected intraperitoneally; the method of administration is described. The dose ranged from 150 to 200 mc., depending on the weight of the patient. Complications from treatment were not troublesome, but 2 patients developed a chronic peritonitis at 10 and 12 months respectively, necessitating laparotomy. The results showed that the palliative use of ^{198}Au to control ascites in 25 advanced cases was successful in preventing ascites in 12 of these. Of one group of 13 patients treated by surgical removal, so far as possible, of the tumour, followed by intra-abdominal injection of ^{198}Au and external irradiation, only 2 had been observed for 2 years, and no conclusions could be drawn from this group. Another group of 12 patients were treated by total hysterectomy, bilateral salpingo-oöphorectomy, and intra-abdominal ^{198}Au. Of 7 of these treated over 2 years ago, 5 are alive and 2 are dead. The 5 other patients were treated less than 2 years ago, and so far all are alive.

The authors consider that the use of ^{198}Au will control the accumulation of ascites in 50 to 70% of advanced cases.

G. B. Goodman

224. **Radioactive Colloidal Gold in the Control of Malignant Effusions. Report and Analysis of 60 Patients**

J. M. Dennis, J. B. Workman, and R. E. Bauer. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 1124–1128, June, 1956. 17 refs.

The authors present an analysis of the results in 60 cases of malignant pleural or peritoneal effusion treated at the University of Maryland Hospital, Baltimore, by the intracavitary injection of radioactive gold (^{198}Au) in doses of 50 to 75 mc. intrapleurally or 100 to 150 mc. intraperitoneally. If necessary, this treatment was repeated after 4 to 6 weeks.

Follow-up records, available in 58 cases, showed that in 36 cases (62%) there was complete cessation of fluid formation for periods ranging from 2 to 15 months, with an average duration of improvement of 5 months. The majority of these patients remained free from troublesome re-accumulation of fluid, and in only 5 cases was repeated instillation of ^{198}Au required. There was no improvement in the remaining 22 cases. The site of the primary tumour was identified in 54 cases, and an attempt was made to correlate the degree of improvement after treatment with the site of the tumour. (In regard to some sites the paucity of numbers precluded any analysis.) Of 17 cases of malignant ascites secondary to ovarian tumour 10, all with large palpable masses, showed no improvement. The authors suggest that in 4 of these cases ^{198}Au may have precipitated intestinal obstruction. In 15 out of 19 cases of pleural effusion secondary to bronchial carcinoma improvement for an average period of 5 months' duration was obtained, while of 8 cases of pleural effusion secondary to carcinoma of the breast, 6 were improved. Only 5 cases of effusion due to lymphoma were treated, and one patient obtained relief for 2 months.

On this experience the authors suggest the following guide to selection of patients if optimal palliation is to be obtained: (1) those in whom fluid formation has become a troublesome problem; (2) those in whom metastases appear as small serosal seedlings rather than large tumour masses; (3) those without severe constitutional effects such as cachexia or anaemia.

G. B. Goodman

Correction:—In the issue for September, 1956, page 244, column 1, line 27, for "left lateral" read "right lateral".

History of Medicine

225. **A Precursor of Hippocratic Medicine.** (Un précurseur de la médecine hippocratique)
V. Gomoiu. *Scalpel* [*Scalpel* (*Brux.*)] **109**, 926–929, Sept. 8, 1956. 3 refs.

226. **On Hysterical and Hypochondriacal Afflictions**
I. Veith. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 233–240, May–June, 1956. Bibliography.

Occasionally some new concept of a disease is proposed which is so revolutionary that it fails both to win acceptance and to exert any influence on subsequent medical thought. Sydenham's theory of hysteria was one such, passing unremarked even in the time of Charcot, whose discoveries it anticipated by two centuries. Rumours that Sydenham had developed such a theory were current in English medical circles late in the 17th century, and at the instance of Dr. William Cole he stated his views in his *Epistolary Dissertation* of 1681–2. From the outset Sydenham states that he regards hysteria as the commonest of diseases, next to fever, and that although women are more afflicted than men, the latter suffer from hypochondriasis, which is as like hysteria " as one egg is to another ", so that the blame cannot be laid on the uterus, as it was by tradition. There follows a description of various types of physical disturbance due to hysteria, with their differential diagnosis, and of the concurrent mental disturbances, emphasizing the patient's deep despair and rapid changes of mood (though here he confuses hysteria with depression). In explanation of these manifestations he postulates a disturbance of the " animal spirits " (*spiritus animales*)—a vague term, of the meaning of which he himself seems to have been somewhat uncertain—which upsets the equilibrium between mind and body and causes local disturbances in the weakest parts of the body.

Sydenham's view that hysteria could occur in both sexes was not original, Piso having already suggested in 1618 that the disease was a purely mental disorder, with no relation to the uterus. Sydenham, however, was probably unaware of Piso's work. His equation of hysteria with hypochondriasis was in keeping with the prevailing tendency to attribute to the hypochondrium in the latter a role similar to that of the uterus in the former, but he based his case on the similarity of the behaviour pattern observed in the two conditions and did not advance any arguments of an anatomical nature, which might have carried more weight with his more tradition-bound colleagues. Nevertheless, the treatment that he advised was entirely along traditional lines, being directed towards relief of the physical symptoms only—by bleeding and purging to rid the body of impurities, and then by " fortifying the blood " with herbal medicines in order to reverse the pathological processes. However, such success as he obtained was probably achieved through his sympathetic handling of his patients rather than through his remedies, which he prescribed with great flexibility according to the special requirements of each case but often discarded altogether, relying only on the healing power of time. *Geoffrey R. Pendrill*

227. **The Contribution of Neisser to the Establishment of the Hansen Bacillus as the Etiologic Agent of Leprosy, and the So-called Hansen–Neisser Controversy**
G. L. Fite and H. W. Wade. *International Journal of Leprosy* [*Int. J. Leprosy*] **23**, 418–428, Oct.–Dec., 1955 [received Aug., 1956]. 9 refs.

Without questioning Hansen's right to be acknowledged as the discoverer of the bacillus *Mycobacterium leprae*, the authors attempt to determine the part played by Neisser in establishing this organism as the aetiological agent in leprosy. At the time of Hansen's discovery (about 1874) the teaching that bacteria cause disease was in its infancy. In 1879 Neisser discovered the gonococcus and demonstrated the leprosy bacillus by newly-introduced staining methods in material supplied to him by Hansen. He concluded his argument for an aetiological significance thus: " Finally, may I repeat that previous authors, notably Hansen, have worked and expressed their views in the same direction. I, for my part, have concerned myself with the demonstration of a wholly specific type of bacterium and its distribution in the organism, which will be found by anyone who seeks it ". In 1880 Hansen, writing for the first time in a language other than Norwegian, contributed an article to a German journal, " partly to maintain priority in this matter before a scientific public larger than the Scandinavian ". In 1881 Neisser retorted that he had " never claimed for himself the priority of having been the first to see bacteria in leprosy ", but had reported a specific type of bacterium aetiologically related to all the lesions of leprosy. He added that he had accorded recognition to Hansen in two places in his short article published in 1879. Neisser's paper of 1881 is an outstanding, definitive description of the relation of the bacilli to the lesions and of their aetiological importance.

Thirty years later (1910) Hansen in his memoirs dealt with this matter briefly and without heat. He realized the German's zeal " to be the first to describe things " and it seemed to him that his paper in the German journal (1880) had for all time established him as discoverer of the aetiological agent of leprosy, which in the literature is called the Hansen bacillus. Neisser on the other hand deserves a secure place in the history of leprosy for confirming and extending Hansen's observations.

The authors point out that most of the literature on leprosy, much of which was written by men personally acquainted with Hansen and Neisser, is devoid of any suggestion of controversy. In their opinion this large volume of negative evidence has weight.

Norman F. Smith